Evaluation of the adequacy of ventilation with low and conventional tidal volumes in overweight and obese adults with normal respiratory function undergoing elective general surgical procedures - a prospective, single-blinded, randomized controlled study.

This Dissertation is in partial fulfillment of the requirement for the M.D. Degree (Branch X) Anaesthesiology Examination of The Tamil Nadu Dr. M. G. R. Medical University, Chennai, to be conducted in April 2011.

C E R T I F I C A T E

This is to certify that the dissertation entitled **'Evaluation of the adequacy of ventilation with low and conventional tidal volumes in overweight or obese patients undergoing elective general surgical procedures - a prospective, single-blinded, randomized controlled study.'** is the bonafide original work of Dr. Justin P. James, towards the M.D. Branch-X (Anaesthesiology) Degree Examination of the Tamil Nadu Dr. M.G.R University, Chennai, to be conducted in April 2011.

Signature of the Guide & H.O.D

Dr. Sarah Ninan
Professor and Head
Department of Anaesthesia
Christian Medical College,
Vellore - 632004.

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CONTENTS

AIM

The aim of this study is to evaluate and compare the adequacy of ventilation with two different tidal volumes (6mL/kg and 10 mL/kg of ideal body weight) in overweight and obese adults undergoing general surgical procedures under general anaesthesia with endotracheal intubation and intermittent positive pressure ventilation (I.P.P.V.).

OBJECTIVES

1. To evaluate the adequacy of ventilation (as evidenced by continuous End-Tidal Carbon Dioxide -$ETCO_2$- monitoring) with two different tidal volumes (6 mL/kg and 10 mL/kg of ideal body weight) in overweight and obese adults undergoing general surgical procedures under general anaesthesia with endotracheal intubation and intermittent positive pressure ventilation.
2. To evaluate the occurrence of ventilation-perfusion mismatch (widening of the P_AO_2-P_aO_2 gradient, decrease in the P_aO_2/F_iO_2 ratio and widening of P_aCO_2-$ETCO_2$ gradient) with two different tidal volumes (6 mL/kg and 10 mL/kg of ideal body weight) in overweight and obese adults undergoing general surgical procedures under general anaesthesia with endotracheal intubation and intermittent positive pressure ventilation.

INTRODUCTION

A large number of surgeries are performed everyday under general anaesthesia with controlled ventilation. The use of general anaesthesia with controlled ventilation has allowed the performance of more and more complex surgical procedures for longer and longer durations. However, this is not without risk. In fact, post-operative respiratory complications form a significant proportion of the post-operative morbidity even after non-thoracic surgery(1)(2). Further, the incidence of post-operative pulmonary complications is more in overweight and obese individuals(2)(3)(4). This has significant implications for anaesthetic practice.

Can improvements in intra-operative ventilatory strategies improve the post-operative outcome? This question has been of interest to researchers for the past several decades. While volume-control ventilation is probably the commonest utilized mode of controlled ventilation, the ideal tidal volume is still a matter of debate. Healthy human lungs seem able to tolerate a wide range of tidal volumes for varying lengths of time. However, there may be subtle changes that, while not manifesting in the intra-operative period, may cause significant post-operative problems.

The issue is further confused by the fact that patients with compromised lung function require different ventilation strategies, which while appearing attractive, may not actually be ideally suited to healthy lungs.

Traditionally, normal tidal volume has been taught as being around 10 mL/kg of the body weight. However, several studies have been done with smaller and larger tidal volumes. Of late, there has been increased interest in the use of lower tidal volumes, perhaps because of fears of barotrauma to lungs subjected to higher tidal volumes. This issue is more significant in overweight or obese individuals where normal tidal volumes (based on actual body weight) may actually be higher tidal volumes (based on ideal body weight)

In the study, we have evaluated the use of low (6 mL/kg of ideal body weight) and conventional (10 mL/kg of ideal body weight) tidal volumes in overweight and obese patients without respiratory illnesses. It has been our attempt to determine the adequacy of these two ventilatory strategies as reflected by the monitoring of end-tidal carbon dioxide levels and arterial blood gas indices of oxygenation.

REVIEW OF LITERATURE

The review of literature is divided into the following topics:

A. History of mechanical ventilation

B. Relevance of I.P.P.V. in anaesthesia

C. Lung volumes

D. Effect of General Anaesthesia on Lung Volumes

E. Controlled Ventilation under Anaesthesia

F. Studies comparing Tidal Volumes

G. Atelectasis under Anaesthesia

H. Obesity, Lung Volumes and Anaesthesia

I. Various Formulae used in this Document

A. HISTORY

The Evolving Understanding of Respiration through the Ages(5)

Even a person without any scientific background intuitively recognizes the necessity of breathing- by its constancy and regularity, by the distress caused by obstructed breathing (whether by asthma or foreign body), or simply by the strong instinct to breath when we try to hold our breath for as long as possible. In that sense, everyone knows the inseparable link between breath and life, but the physiology behind it is complex, and it is enlightening as well as entertaining to learn of how the human race grew in its understanding of this process.

Early Greco-Roman Era

The early understanding of respiration was innately linked to the understanding of circulation. The ancient Greeks, including Galen and Aristotle, believed that the heart was like an engine that distributed energy (as innate heat) to the body and that the lungs functioned to cool the heart by the constant passage of air. The anatomical relationships of the lungs, pulmonary circulation, systemic circulation, and heart were not well understood. In the second century A.D., Galen was arguably the most influential physician in Greco-Roman culture. He advanced their understanding of respiration a little further by suggesting that air was carried by blood to all tissues, and that blood carried wastes to the lungs to be discharged into the atmosphere.

Renaissance Era Physicians

There was little advancement in this field of knowledge from Galen's times till the 15th and 16th century. Interest in anatomy was triggered by Renaissance artists like Leonardo da Vinci who strived for accuracy in their artistic depictions. This interest was carried forward by prominent physicians like Vesalius. Servetus was the first to suggest that blood changed

colour during passage through the lungs and that this was the result of mixture of blood with inspired air and the removal of 'sooty vapours'. In the early 17th century, William Harvey, who is famous for elucidating the circular nature of blood flow, suggested as a direct result of his findings, that blood must traverse the lung tissue through tiny channels. Marcello Malpighi then provided the next link in the chain of discovery around 1650 using microscopes to study tissues. He explained that air passes into microscopic sacs in the lung but does not physically come into contact with blood which travels through capillaries connecting arteries and veins. The final piece of the puzzle was put in place by a contribution from the field of physical chemistry when the process of diffusion of air across membranes was described.

Chemists and Physiologists

The 17th and 18th centuries also saw the development of understanding that air was composed of different gases with differing properties. Specifically, they determined the existence carbon dioxide that was found in exhaled air and would not support combustion or life, and oxygen that would support both. The work of many scientists, including Antoine Lavoisier and Robert Boyle, proved that life processes required the utilization of oxygen for reactions similar to combustion (and the resultant production of carbon dioxide) in the peripheral tissues. In the first half of the 19th century, devices were invented for measuring the content of oxygen and carbon dioxide in blood- the precursors of our modern blood gas analysers. However, it wasn't until the second half of the 20th century that practical electrodes were developed for measuring oxygen and carbon dioxide tensions in solutions. The significance of pH wasn't widely accepted till the work of Bjorn Ibsen during the Polio epidemic in Copenhagen in 1952 relating respiratory insufficiency, hypercapnia and acidosis. As a result of all these developments, the first commercial blood gas analyser measuring pH, PaO2 and PaCO2- the ABL1 by Radiometer, was available in 1973.

History of Endotracheal Intubation and Mechanical Ventilation(5)(6)

Galen

The history of intubation and ventilation also starts with Galen. He first demonstrated that it was possible to inflate a dead animal's lungs by passing a reed into the trachea and blowing air through it. Of course, he did not know what the purpose of ventilation was, and his knowledge of the topic extended no further. During his work on dissection of animals, he found that the animal would die shortly after their chest cavity was opened, preventing him from observing the beating heart in action.

Vesalius and Vivisection

Almost one and a half millennia later, Andreas Vesalius, the father of anatomy, faced the same problem. He too chanced upon the technique of blowing air into the animal's lungs with a reed placed in the trachea. But his work went further, because he noticed that when he performed this manoeuvre on animals whose heart had almost stopped beating after a thoracotomy, their heart would start beating again. In 1664, Robert Hooke later showed that an animal's heart could be kept beating for over an hour by this technique. His colleague, Richard Lower, further demonstrated that on ventilating the lungs, blood would retain its bright red colour instead of taking on a darker blue shade. Though this method of keeping animals alive proved very helpful to the field of animal vivisection, its use in human beings was not to be for over another hundred years.

Advent of Positive-Pressure Ventilation

In the middle of the 18th century, the first attempts at revival of drowning victims were recorded. These attempts included mouth-to-mouth resuscitation. Soon, this advanced to the use of tracheal tubes and bellows for positive-pressure ventilation. These developments led to

the formation of, and were later encouraged by, the Royal Humane Society. However, positive-pressure ventilation soon recieved a severe setback. In 1827, J. Leroy conducted a series of dramatic experiments where he caused fatal pneumothorax in animals by overzealous positive-pressure ventilation. Without knowledge of the high airway pressures attained in the experiment, positive-pressure ventilation came into disrepute and was soon condemned and abandoned in patients. However, it continued to be popular in the laboratory for animal experiments. For almost the next hundred years, medical science would meander through the use of negative-pressure ventilation.

Negative-Pressure Ventilators

Negative-pressure ventilators, including the famous Iron-Lung, came to be used very widely in various conditions associated with respiratory insufficiency, most notably polio-induced respiratory paralysis. Doubtless, they saved many lives. However, they were very large and cumbersome (metal chambers covering the trunk or entire body) and made nursing care and surgical interventions very difficult. In fact, to facilitate surgery, some negative-pressure ventilators were made as large as a room, allowing the surgeon to stand inside. Only the patient's head would be outside the room to allow the pressure difference to enable airflow.

Re-emergence of Positive-Pressure Ventilation

By the end of the 19th century, various surgical procedures were being performed under anaesthesia with the widespread use of inhalational agents. Ether and Chloroform were delivered by dropping onto a gauze piece placed over an ether mask (Open Drop method) and the vapours were inhaled by the spontaneously-breathing patient. While this method was adequate for most peripheral procedures, and upper abdominal procedures were merely difficult due to the irregular movement of patient breathing, intra-thoracic procedures were near-impossible due to the “pneumothorax problem.”

Opening the thoracic cavity resulted in a loss of negative intra-pleural pressure on the same side and a consequent collapse of the ipsilateral lung. The term “Pendelluft” was used to describe the to-and-fro movement of air between the two lungs with paradoxical motion of the collapsed lung. This situation was not physiologically sustainable and would rapidly degenerate to hypoxic arrest- the same problem encountered by Galen and Vesalius centuries before. Thus, intra-thoracic surgeries were limited to extremely short procedures, and the mortality associated with thoracic surgery was very high. It was obvious that the solution lay in ventilating the lungs effectively. Two methods were suggested- negative-pressure ventilation with the body inside a negative-pressure chamber, and positive-pressure ventilation with the head inside a positive-pressure box. What's interesting to note is that neither method involved intubation of the trachea. This was because, at the turn of the 20th century, intubation for intra-operative management was still viewed with scepticism.

Actually, airway control had been in use already for several years. Snow, in 1858, had anesthetized rabbits with Chloroform via a tracheostomy tube. Trendelenburg had devised a cuffed tracheostomy tube for use in patients undergoing oral and laryngeal surgeries. This prevented aspiration of blood and tissue debris, and necessitated administration of inhalational agents through the tracheostomy tube. In 1880, MacEwen developed an uncuffed metal oro-tracheal tube for upper airway obstruction. Within a few years, Joseph O'Dwyer, a paediatrician also devised an uncuffed metal oro-tracheal tube to treat children with Diphtheric airway obstruction. A surgeon named Fell had invented a bellows system for positive-pressure ventilation. Fell and O'Dwyer combined their inventions to produce the Fell-O'Dwyer apparatus which they used to ventilate apnoeic drug-overdose patients. As early as the turn of the century, Matas used the Fell-O'Dwyer apparatus for thoracic surgery. However, these instances were the exception rather than the rule because tracheostomy was

obviously too invasive for elective procedures, uncuffed oro-tracheal tubes did not solve the problem of aspiration, and most of the intubations described till date had been “blind” ones.

The next three decades saw the development of practical laryngoscopes (Kirstein, Jackson) and cuffed endotracheal tubes (Dorrance, Guedel). By 1934, Guedel and Treweek showed that hyperventilating a patient and deep plane of anaesthesia resulted in apnoea so that ventilation could be controlled by manual bag ventilation and provide a quiet surgical field. Despite all these developments, endotracheal intubation and controlled ventilation were not widely accepted till the advent of non-depolarizing muscle relaxants in the 1940s.

Mechanical ventilators had been devised in the first half of the 20th century for use in apnoeic patients. Devices for providing intermittent positive pressure ventilation (I.P.P.V.) were also developed for military purposes and later introduced to the medical field. During the polio epidemic in Copenhagen in 1952, Bjorn Ibsen, an anaesthesiologist, conclusively showed that ventilation could dramatically reduce mortality. With the number of negative-pressure ventilators available being grossly inadequate for the number of patients, Ibsen turned to manual bag (positive-pressure) ventilation. It is estimated that as many as 1500 medical and dental students were recruited to provide round-the-clock bag ventilation to these patients. The Copenhagen epidemic fuelled interest in the development of mechanical positive-pressure ventilators and also in the development of I.C.U.s (intensive care units) where sick patients requiring mechanical ventilation could be grouped together and cared for in a specific manner.

B. RELEVANCE OF I.P.P.V. IN ANAESTHESIA

Endo-tracheal intubation and mechanical ventilation is just one of many modes of respiratory management under general anaesthesia. The other modes of management include:

1. Supplementary oxygen via face mask during Total Intra-Venous Anaesthesia (T.I.V.A.);
2. Mask-holding with spontaneous inhalation of anaesthetic;
3. Bag-mask ventilation with/ without paralysis;
4. Supra-glottic airway device used with spontaneous respiration;
5. Supra-glottic airway device used with controlled/ assisted ventilation;
6. Endo-tracheal intubation with spontaneous ventilation.

Endo-tracheal intubation and controlled ventilation offer several advantages during the peri-operative period. Some of these are:

1. Protection of lung from aspiration;
2. Prevention of patient movement;
3. Reduces patient effort;
4. Adjustment of ventilator settings to manipulate carbon dioxide levels in the blood;
5. Allows use of lighter planes of anaesthesia due to concomitant use of muscle relaxants.

For these and other reasons, controlled ventilation with an endotracheal tube is preferred for a large variety of situations under general anaesthesia including:

1. Patients with airway compromise;

2. Patients with respiratory distress or insufficiency;
3. Patients with poor lung compliance;
4. Patients with haemodynamic instability;
5. Long-duration procedures;
6. Situations where aspiration of extraneous material into the airway is a concern;
7. Procedures where lack of patient movement is essential / preferable;
8. Most laparoscopic, upper abdominal, intra-thoracic, intra-cranial and airway surgery.

However, there are disadvantages to the technique when compared with other technique of respiratory management under general anaesthesia. These include:

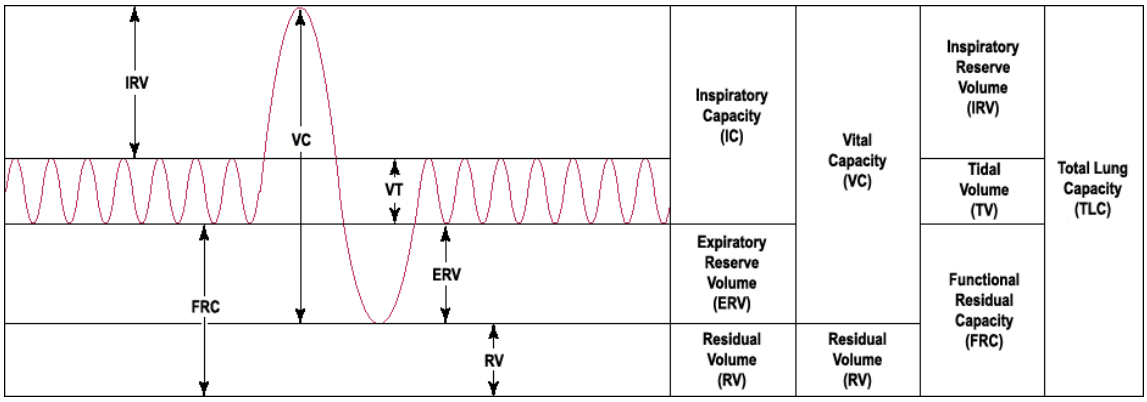
1. Greater haemodynamic alterations during insertion and removal;
2. More likelihood of trauma to airway structures;
3. Needs use of muscle relaxant to prevent ventilator-patient dys-synchrony;
4. Possibility of barotrauma.

C. LUNG VOLUMES(7)(8)

The various lung volumes are shown in **Fig. 1.** The various volumes and capacities are about 20-25 % smaller for women than for men of the same age, and larger for taller and more athletic people than for shorter or less athletic people of the same age. They are as follows:

- Tidal Volume: The volume of air breathed in or out during quiet breathing. It has been measured as being 6-8 mL/kg or about 500 mL in an adult male.
- Inspiratory Reserve Volume: The volume of air inspired in addition to the tidal volume on making maximum effort after a tidal expiration. It is about 3000 mL in a normal adult male.

FIG. 1: NORMAL LUNG VOLUMES.



- Inspiratory Capacity: The sum of tidal volume and inspiratory reserve volume is normally around 3.5 litres.
- Expiratory Reserve Volume: The volume of air exhaled in addition to the tidal volume on maximum effort after a tidal inspiration. It is about 1100 mL in an adult male
- Vital Capacity: The maximum volume that can be inhaled after a maximal exhalation or the maximal volume that can be exhaled after a maximal inspiration. It is the sum of tidal, inspiratory reserve, and expiratory reserve volumes and measures about 60-70 mL/kg or 4600 mL in an adult male.
- Residual Volume: Volume of air remaining in the lungs after a maximal exhalation. It is about 1200 mL in a normal adult male.
- Functional Residual Capacity: It is the volume of air remaining in the lungs at the end of a tidal exhalation and is the sum of residual and expiratory reserve volume. It is about 2300 mL in an adult male.

- Total Lung Capacity: It is the maximum volume to which the lungs can be inflated by a person's own effort. It is the sum of vital capacity and residual volume and is around 5.8 litres in an adult male.

D. EFFECT OF GENERAL ANAESTHESIA ON LUNG VOLUMES(9)

General anaesthesia invariably results in a reduction in the Functional Residual Capacity (F.R.C.). This is in addition to the reduction in F.R.C. seen on changing from erect to supine position. This is probably caused by loss of skeletal muscle tone affecting the respiratory muscles resulting in a cranial shifting of the diaphragm's resting position and also a decrease in the transverse thoracic area. The average reduction is about 20% of the awake F.R.C. This reduction occurs at induction and does not increase with muscle paralysis and controlled ventilation.

E. CONTROLLED VENTILATION UNDER ANAESTHESIA

Controlled ventilation is utilized very commonly under general anaesthesia due to the many advantages mentioned earlier. Ventilators attached to the latest anaesthesia workstations are very advanced and allow various modes of ventilation. However, the earliest ventilators were stand-alone devices which often had only volume-control mode of ventilation. Even today, simple volume-control ventilators are probably the most commonly used ventilators, especially where finances are not plentiful. Indeed, the simplest modes, volume-control and pressure-control, are more than adequate for most patients undergoing most surgical procedures. Thus, for reasons of availability, economy, familiarity, and adequacy, volume-control ventilation is the most commonly used mode.

F. STUDIES COMPARING TIDAL VOLUMES

Traditionally, tidal volumes of 10 mL/kg or more have been used during controlled ventilation(7)(10)(11)(12)(13)(14)(15). A significant proportion of patients receiving controlled ventilation are those with lung injury due to various reasons. Growing suspicion that controlled ventilation worsens pre-existing lung injury lead to experimentation with ventilatory parameters including tidal volume. A number of studies compared lower tidal volumes, usually around 6-7 mL/kg, with conventional tidal volumes of 10 mL/kg(16) in patients fulfilling the criteria(17) for acute lung injury (A.L.I.) or acute respiratory distress syndrome (A.R.D.S.) or at high risk for the same. While these studies produced inconclusive results showing no difference in major outcome variables, there was nonetheless, a growing interest in limiting tidal volumes to reduce damage caused by overdistention. This was even recommended by a consensus conference in 1993(18).

In May 2000, the New England Journal of Medicine published the landmark study(19) of the Acute Respiratory Distress Syndrome Network (ARDSNet) which showed that lower tidal volumes decreased mortality and duration of mechanical ventilation in patients with A.L.I. and A.R.D.S(19)(20). The issue is far from settled and various subsequent publications have questioned the validity of the conclusions drawn from this study(11). It has been suggested that the main difference in intervention that reduces mortality is not a specific tidal volume, but the limitation of plateau pressures(16).

Nonetheless, it cannot be denied that the article in question has had a significant impact on ventilatory practices throughout the world. There has been a change in practice in ventilation strategies being followed in intensive care units, where a significant proportion of patients have compromised lung function(21)(22). Such practices are extending into the peri-operative setting, and more patients are being ventilated with lower tidal volumes under

anaesthesia. However, it must not be forgotten that most patients we come across in the field of anaesthesiology have normal lung function, in contrast to most patients requiring ventilation in an intensive care unit. The effect of lower tidal volumes on patients with normal lung function is unclear. There is no real evidence that such a practice may be beneficial in patients with normal respiratory function. Further, it should be noted that the ARDSNet study(19) was performed using P.E.E.P. (Positive End-Expiratory Pressure). Indeed, most patients with pre-existing lung-injury are ventilated with, and do better with, the use of P.E.E.P., sometimes at very high levels. However, the use of P.E.E.P. in patients with normal respiratory function undergoing anaesthesia is uncommon, mostly because it is considered unnecessary(23) and is not without adverse effects(9).

Visick et al(24) and Tweed et al(25) have advocated the use of larger tidal volumes in patients with no pre-existing lung injury. More recently, however, Cai et al(26) have suggested that low tidal volumes are no different from conventional tidal volumes and Wolthuis et al(27) have suggested that the use of low tidal volumes may even be protective for normal lungs.

Some studies comparing low and high tidal volumes have used tidal volumes that would today be considered unphysiological. For example, Caruso et al(28) compared tidal volumes of 6 mL/kg and 24 mL/kg while Bardoczky et al(29) compared tidal volumes of 13 mL/kg to 22 mL/kg. Since such volumes are extremely unlikely to be used in clinical practice, the significance of such studies to the topic in question is put in doubt.

Studies comparing different tidal volumes have used various parameters to determine harm or benefit. These include arterial blood gas analysis(30)(31), computed tomography (C.T. scan)(30)(32), and evidence of inflammation(33)(34)(28)(27). Arterial blood gas analysis is used to determine and compare indices of oxygenation, Computed Tomography is

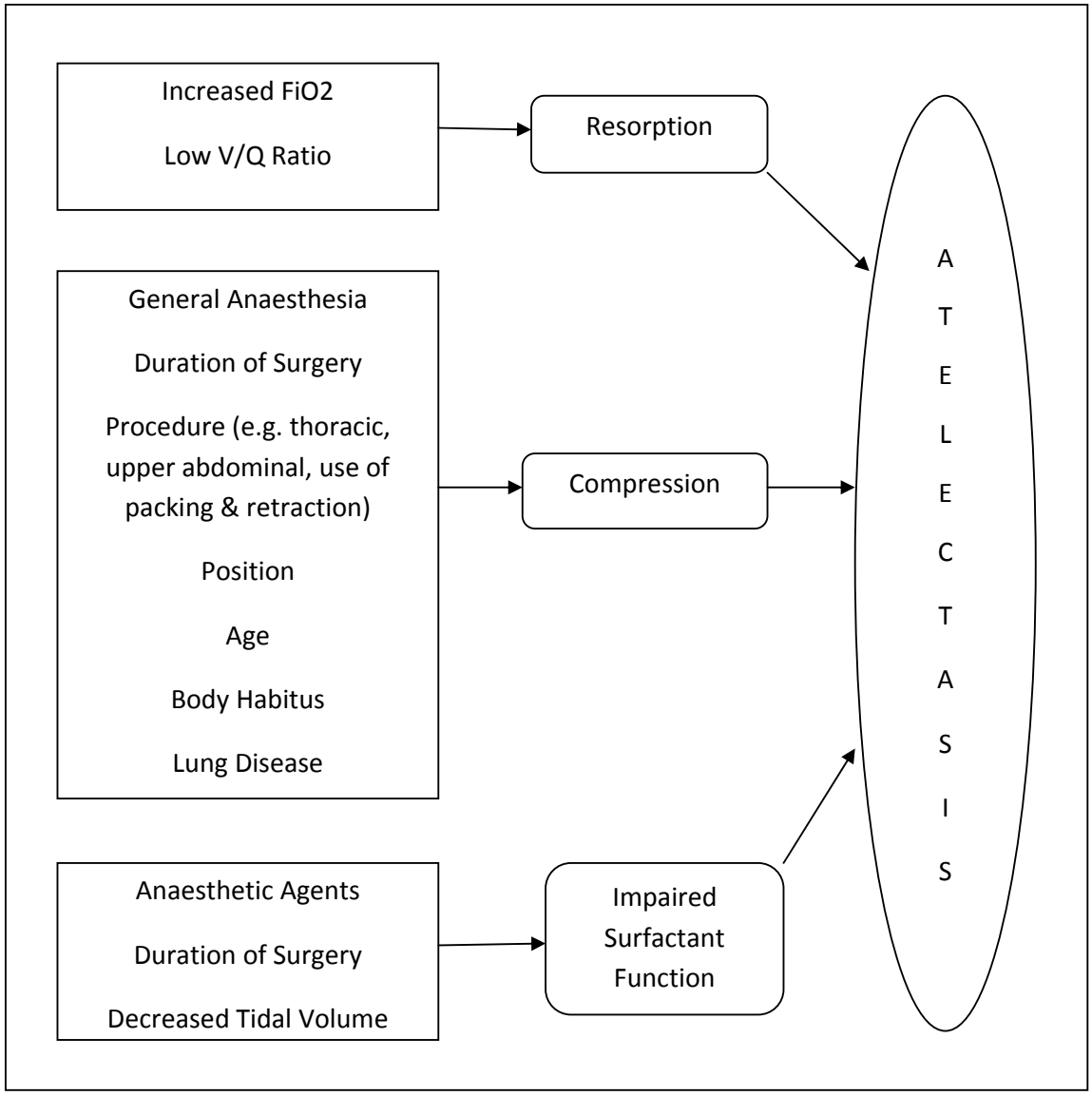
used to measure the volume of atelectasis developing in the lungs, and evidence of inflammation is gathered by histological examination of lung tissue and comparing local (pulmonary) and systemic levels of various endogenous mediators of inflammation like Interleukins and cytokines.

G. ATELECTASIS UNDER ANAESTHESIA(35)(9)

Atelectasis is defined as collapse of lung tissue affecting all or part of the lung. Three different mechanisms(36)(37) have been proposed that may cause or contribute to atelectasis. These mechanisms are applicable under anaesthesia also.

1. *Compression Atelectasis*: occurs when the transmural pressure reduces to such a level that it is unable to prevent the tendency of the alveoli to collapse. Under anaesthesia, this is mostly due to decreased diaphragmatic tone and cephalad displacement of the diaphragm. Other contributing factors include change in the chest wall geometry and pooling of peripheral blood in the abdominal cavity pushing the diaphragm further up.
2. *Resorption Atelecatsis*: (Gas Atelectasis) occurs by two mechanisms. First, when smaller airways leading to alveolar units are closed, the gas trapped in the alveoli gradually gets absorbed by the blood. With no new gas entering the alveoli, they collapse. Second, in alveolar units where the F_iO_2 is high and the V/Q (ventilation-perfusion) ratio is low, uptake of gas into the bloodstream is faster than entry of new gas into the alveoli causing a progressive depletion of alveolar volume and finally, collapse.
3. *Surfactant Impairment*: Surfactant is chiefly composed of phospholipids. It coats the surface of alveoli and serves to reduce the surface tension, and thus prevents collapse

FIG 2: MECHANISMS OF ATELECTASIS UNDER ANAESTHESIA(37)



of the alveoli. Impaired surfactant formation or function can lead to atelectasis. It has been shown that anaesthesia impairs surfactant function.

All three mechanisms may be operational and contributory to the atelectasis seen in the peri-operative setting. This is summarized in **Fig 2**. Atelectasis was first described in the

peri-operative setting in 1928 by Lee et al(38) who described it as a post-operative complication. In 1963, Bendixen et al(39) noticed a progressive decline in compliance of the respiratory system as well as in P_aO_2 under anaesthesia and suggested that it was due to atelectasis. In 1985, Brismar et al(40), studying CT (Computerized Tomography) changes in lung tissue under anaesthesia, noted that within five minutes of induction, areas of increased density appeared in the dependant regions of the lungs. They suggested that the densities (from -100 to +100 Hounsfield units) represented atelectasis(32).

Further investigation has borne out their theory and today, it is known that nearly 90% of all patients develop some amount of atelectasis under anaesthesia(32)(35). It is also known that the amount of atelectasis increases with the use of low tidal volume ventilation(41), use of higher F_iO_2(42), and in obese patients(43)(4). Atelectasis causes an increase in the ventilation-perfusion mismatch. Specifically, it causes an increase in shunt(36)(37) which is a situation where blood flow occurs through pulmonary capillaries without gas flow in the corresponding alveolar units. The gas-exchange impairment has been correlated with the degree of atelectasis(30)(35)(43)(44), and even a mathematical relationship has been suggested:

Shunt = (0.8 × Atelectasis) + 1.7 (9)(45)

Where: Shunt- expressed as percentage of cardiac output; and

Atelectasis- expressed as percentage of lung area.

This atelectasis can reasonably be expected to raise the alveolar-arterial oxygen gradient and arterial oxygen-inspired oxygen ratio(46), and possibly the arterial- end-tidal carbon dioxide gradient. These changes can be easily detected by an arterial blood gas analysis.

Atelectasis is related to post-operative pulmonary complications(47)(48) as a cause of hypoxaemia(35)(36) and as a focus of infection(49). The respiratory system is the source of most post-operative complications following non-cardiac surgery(1) and these can be attributed, to at least some extent, to atelectasis(36). Post-operative pulmonary complications (incidence about 4% of elective surgery(50)) have a significant impact on morbidity, mortality, duration of hospital stay, and cost of health care(35)(47)(2). Also, these complications are more likely in obese patients(36)(51).

Several methods have been described to prevent or treat atelectasis(9)(36)(37). Some of these are:

1. *Use of P.E.E.P.*: has been shown to reduce the amount of atelectasis, although it does not eliminate it completely. However, this method is not ideal for several reasons. P.E.E.P. has its own problems. It increases dead-space ventilation, and it reduces venous return and thus, the cardiac output. Further, the recruited lung units collapse almost immediately on cessation of P.E.E.P.
2. *Maintenance of Muscle Tone*: prevents atelectasis. Ketamine, which does not impair muscle tone, does not lead to formation of atelectasis as long as muscle relaxants are not used. Phrenic nerve stimulation, to maintain diaphragmatic muscle tone, has also been shown to reduce atelectasis.
3. *Use of lower F_iO_2*: High F_iO_2 is often used in the beginning of anaesthesia to provide a safety margin in case of a difficult airway. This has been shown to increase the amount of atelectasis. Use of lower F_iO_2 during anaesthesia may be recommended.
4. *Recruitment Manoeuvres*: Inflating lungs to 40 cm H_2O and maintaining the inflation for 7-8 seconds(36) re-opens collapsed lung units. This, however, can have haemodynamic consequences. Also, atelectasis reappears shortly.

Interestingly, the first methods used to prevent or reduce the formation of atelectasis under anaesthesia were the use of larger tidal volumes(7) (which is why conventional tidal volumes during mechanical ventilation are 10 mL/kg body weight even though resting awake spontaneous tidal volumes in normal adults is 6-8 mL/kg body weight) and the “Sigh” button on older mechanical ventilators, which delivered a larger tidal volume over a longer period of time (than the ventilator settings) at regular intervals to open up collapsed lung units.

H. OBESITY, LUNG VOLUMES AND ANAESTHESIA

The obvious anaesthetic implications of obesity in the respiratory system include Obstructive Sleep Apnoea (O.S.A.) and concerns about a difficult airway. With regard to lung volumes, obesity is associated with reductions in the Total Lung Capacity (T.L.C.), Functional Residual Capacity (F.R.C.) and Expiratory Reserve Volume (E.R.V.)(3). This is shown in **Figure 3**. This has been attributed to the relative upward displacement of the diaphragm and its decreased excursion due to accumulation of adipose tissue in the abdominal cavity. Often, the F.R.C. drops below the Closing Capacity resulting in small airway closure and ventilation-perfusion mismatch leading on to arterial hypoxaemia.

The reduction in F.R.C. is worsened under anaesthesia as shown in **Figure 4**. In fact the F.R.C. may be reduced by as much as 50% in morbidly obese patients under anaesthesia compared to a 20% reduction in F.R.C. in normal adults(53). This means such patients have a lower reserve of oxygen for periods of apnoea such as during induction and airway manipulation resulting in a greater incidence of hypoxaemia and desaturation under anaesthesia. Methods to increase the F.R.C. include controlled ventilation with larger tidal volumes and the use of P.E.E.P. (Positive End-Expiratory Pressure). Of these two, P.E.E.P.

increases the F.R.C. more but at the cost of decreased cardiac output and decreased systemic oxygen delivery(9).

FIG. 3: CHANGE IN LUNG VOLUMES WITH OBESITY(52)

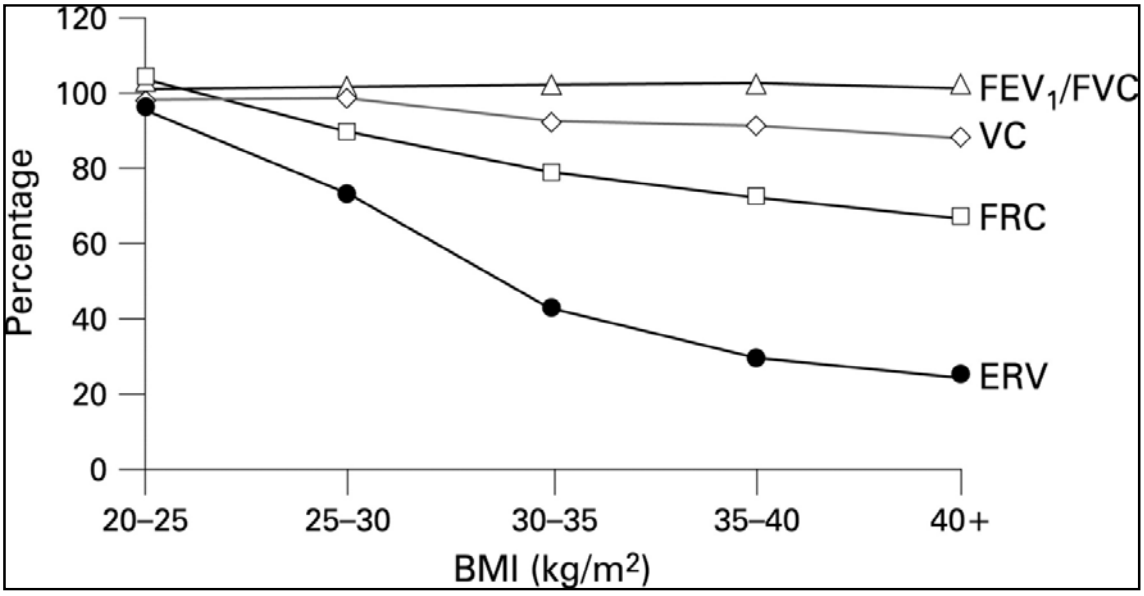
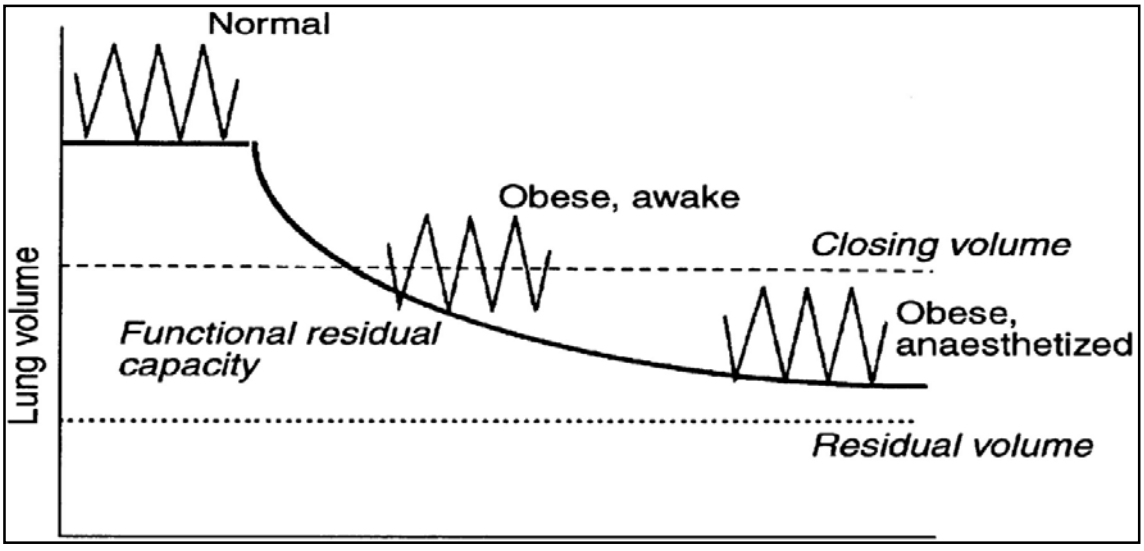


FIG. 4: DECREASING F.R.C. IN OBESE UNDER ANAESTHESIA(3)



I. VARIOUS FORMULAE USED IN THIS DOCUMENT

1. *Classification of Obesity based on Body Mass Index*: The classification of *overweight* as a Body Mass Index (B.M.I.) of 25.0 or more, and *obese* as a B.M.I. of 30.0 or more is based on the W.H.O. (World Health Organisation) B.M.I. cut-off points(54) which is an international classification.

2. *Calculation of Ideal Body Weight*: The formula for Ideal Body Weight (I.B.W.) has been taken from Lemmens et al(55), which correlates well with other published formulae derived for the same purpose. The formula is

   IBW (ideal body weight) = 22 x [Height (in metres)]^2

   The concept of ideal body weight arose from weight tables created by insurance companies in an attempt to link body weight and mortality. Subsequently, various formulae have been given to calculate ideal body weight. This particular formula simply gives the body weight at which the individual would have a B.M.I. (Body Mass Index) of 22 which lies exactly midway through the normal range of B.M.I. (19.0 to 24.9).

3. *Alveolar Gas Equation*: The formula is given as

   $P_AO_2 = [F_iO_2 \times (760 - 47)] - [P_ACO_2/R] + [P_ACO_2 \times F_iO_2 \times \{(1 - R)/R\}]$ (56)

   where P_AO_2 : partial pressure of oxygen in alveolar gas (mm Hg)

   F_iO_2 : oxygen concentration of inspired gas mixture (%)

   760 : atmospheric pressure (mm Hg)

   47 : partial pressure of water vapour in atmospheric air (mm Hg)

   P_ACO_2 : partial pressure of carbon dioxide in alveolar gas (mm Hg)

R : respiratory quotient

The assumptions made in this formula are:

a. There is no CO_2 in the inspired gas mixture. This is ensured by the use of CO_2 absorber with the circle system.
b. $P_ACO_2 = P_aCO_2$. Alveolar and arterial partial pressures of carbon dioxide are the same if respiratory function is normal. However, this assumption may be incorrect if significant shunt is present, when arterial PCO_2 is higher than alveolar PCO_2.
c. Respiratory Quotient (R) is assumed to be 0.8 under normal metabolic conditions. It can, in reality vary from 0.7 to 1.0 depending on the metabolic activity and diet.

METHODOLOGY

INTERVENTION AND PROCEDURE IN DETAIL

This study compares two different tidal volumes during ventilation under anaesthesia. Informed consent is obtained prior to transferring the patient into the operating room. Standard monitoring is established as indicated for the procedure including continuous end-tidal carbon dioxide monitoring ($ETCO_2$). A standard general anaesthetic is administered with standard drugs. The dosage of drugs and the use of additional regional techniques for anaesthesia / analgesia are decided by the primary care-giver anaesthesiologist.

Continuous $ETCO_2$ monitoring is performed from the point of induction. Volume-controlled ventilation is provided with the anaesthesia ventilator built into the Datex-Ohmeda Aestiva/5 workstation via a circle system. The tidal volumes are 6 mL/kg and 10 mL/kg of the IBW (ideal body weight) in the two arms (called Group I and Group II respectively) of the study.

IBW is determined by the formula:

$$IBW = 22 \times [\text{Height (in metres)}]^2 \quad (55)$$

The tidal volume is then calculated and rounded off to the nearest 25 mL based on the group to which the patient is randomized. The respiratory rate is set at 12 bpm (breaths per

minute) initially. The upper pressure limit is set at 35 cm H_2O to avoid barotrauma. The F_iO_2 is set at 0.6 as far as possible.

After induction, intubation and confirming air entry, the circle system is connected to the ventilator and the ventilator is activated. An ABG (arterial blood gas) analysis is performed immediately after initiating controlled ventilation. This is called Sample A. The $ETCO_2$ at the time of collecting the arterial blood sample is noted. The arterial sample is collected with the smallest possible needle (preferably 26 gauge) from the radial artery at the wrist unless the patient already has an arterial cannula inserted for monitoring. The site of collection is compressed and a compressive dressing is placed. At the end of the procedure, the site is checked for bleeding and palpability of the pulse.

The P_AO_2 (partial pressure of oxygen in the alveoli) is calculated using the formula:

$$P_AO_2 = [F_iO_2 \times (760 - 47)] - [P_ACO_2/R] + [P_ACO_2 \times F_iO_2 \times \{(1 - R)/R\}] \quad (56)$$

Where: R (respiratory quotient) = 0.8 (under normal metabolic conditions); and

P_ACO_2 (alveolar) = P_aCO_2 (with normal respiratory function)

Thus, the P_AO_2-P_aO_2 (alveolar-arterial oxygen) gradient, the PaO_2-F_iO_2 ratio, and the P_aCO_2-$ETCO_2$ (arterial to end-tidal carbon dioxide) gradient can be determined. Another ABG analysis is performed two hours after the first ABG with similar precautions as mentioned before. This is called Sample B. The above-mentioned gradients are calculated once more. Development of primary respiratory acidosis or alkalosis is also noted.

During the procedure, anaesthesia, analgesia, and muscle relaxation is as per the care-giver's decision following existing standards of care.

Continuous $ETCO_2$ (end-tidal carbon-dioxide) monitoring is performed. Allowable upper and lower limits of $ETCO_2$ are predetermined (upper limit- 40 mm Hg; lower limit- 24 mm Hg). If the monitored $ETCO_2$ goes beyond the set limits, the respiratory rate is changed

to bring the $ETCO_2$ back to the acceptable range. The rate is increased by 2 bpm at a time if the $ETCO_2$ rises and decreased at a similar rate if the $ETCO_2$ falls. The need to change the respiratory rate is noted. If the $ETCO_2$ does not come back to the acceptable range despite changing the respiratory rate to 18 bpm or 6 bpm, the tidal volume is changed similarly by 50 mL at a time.

Any clinically significant abnormality detected on ABG is treated as required. Respiratory acidosis is treated with hyperventilation and respiratory alkalosis with decreased ventilation. Any indication of atelectasis (decrease in oxygenation) is treated with a vital capacity manoeuvre (manual inflation upto 40 cm H_2O maintained for 7-8 seconds). After collecting the second ABG, ventilatory settings are re-adjusted as deemed necessary by the primary care-giver.

Withdrawal of anaesthesia, reversal of neuro-muscular blockade, extubation and post-operative care is carried out as per existing standards of care.

KEY INCLUSION / EXCLUSION CRITERIA

Inclusion Criteria:

ASA (American Society of Anaesthesia) physical status 1 & 2 adult patients with a BMI (body mass index) of 25 or more undergoing general surgical procedures under general anaesthesia with IPPV.

Exclusion Criteria:

1. ASA physical status 3 & 4;
2. Age less than 18 years or more than 75 years;

3. BMI of less than 25;
4. Known case of bronchial asthma, COPD (chronic obstructive pulmonary disease), or other respiratory pathology;
5. Pre-existing acid-base abnormality;
6. Patients with a history of smoking;
7. Laparoscopic procedures;
8. Emergency procedures;
9. Procedures involving thoracotomy or alteration of ventilatory parameters for surgical purposes;
10. Procedures expected to last for less than 2 hours duration;
11. Refusal / inability to give consent.

SETTING OF THE STUDY

The study is carried out under the Department of Anaesthesiology, Christian Medical College, Vellore in the main Operating Theatre complex. The subjects are taken from among patients coming for elective surgery under the Department of General Surgery.

STUDY DESIGN

The study is a randomized controlled trial involving two arms (or groups). Patients are randomly selected to either arm of the study. The two arms are named Group I (where patients receive tidal volumes of 6 mL/kg) and Group II (where patients receive tidal volumes of 10 mL/kg).

METHOD OF RANDOMIZATION

Subjects are assigned to the study groups using simple randomization. The groups to which the patients are to be allocated are written on pieces of paper in equal numbers and placed in opaque envelopes. The envelopes are mixed in a bag. An envelope is taken from the bag before the start of each case and the envelope opened to determine the group to which the patient is allocated. The calculation of initial tidal volume is done after this.

METHOD OF ALLOCATION CONCEALMENT

Allocation is concealed using opaque envelopes.

BLINDING AND MASKING

The study is single-blinded. The patient will be unaware of which group he / she is placed in. We are unable to perform double-blinding under the circumstances as the investigator is the one setting the ventilator controls (tidal volume and respiratory rate).

OUTCOMES

Primary Outcome:

$ETCO_2$ surpassing allowable limits and requiring a change in respiratory rate and tidal volume for normalization.

Secondary Outcomes:

1. Any respiratory acid-base abnormality.

2. Change in the P_AO_2-P_aO_2 gradient,

3. Change in the P_AO_2-F_iO_2 ratio,

4. Change in the P_aCO_2-$ETCO_2$ gradient.

TARGET SAMPLE SIZE AND RATIONALE

A pilot study was carried out to determine the sample size.

Based on the pilot study:

Patients in 6mL/kg group expected to have primary outcome = 75%

Patients in 10mL/kg group expected to have primary outcome = 30%

Thus, expected difference = 45%

Significance level = 5%

Power = 80%

Thus, based on the formula: $$(Z_\alpha + Z_\beta)^2 \frac{[P_1(1-P_1) + P_2(1-P_2)]}{d^2}$$

Sample size = 18 in each group,

= 36 patients in total.

STATISTICAL ANALYSES

Descriptive statistical methods like mean, standard deviation and confidence intervals is calculated for the baseline variables in each group.

The primary outcome is the occurrence of inadequate ventilation as defined by abnormal $ETCO_2$. This outcome variable is compared between the two groups using Chi-Square tests to determine statistical significance.

For the continuous variables, mean difference between the groups is compared using the Two-Sample T Test for independent and paired samples.

All data analysis is performed using the software SPSS 14.0 and Microsoft Office Excel 2007.

RESULTS

The two groups in this study are Group I (6 mL/kg) and Group II (10 mL/kg). There are 19 patients in Group I and 17 patients in Group II making a total of 36 patients.

DEMOGRAPHIC VARIABLES

The demographic variables are listed in **Table 1**. All demographic variables are equally distributed in the two groups. As can be seen from the p-Values given in **Table 1**, there is no significant difference in the distribution of the various demographic variables between the two intervention groups.

The average age in Group I is 43.16 years and in Group II is 46 years.

There are 4 males in Group I and 3 males in Group II. The percentage distribution of males and females is similar in the two groups.

The average weight of the patients in Group I is 72.79 kg. The weights range from 57 kg to 96 kg. In Group II, the average weight of the patients is 69.58 kg and the range is from 58 kg to 100 kg.

The average height in Group I is 1.58 m and in Group II is 1.56 m.

TABLE 1: DEMOGRAPHIC VARIABLES

VARIABLE	GROUP I (6 mL/kg)	GROUP II (10 mL/kg)	**p Value** (difference between Group I & Group II)	ALL PATIENTS
Age (Years)	43.16 ± 8.95*	46 ± 12.25*	**0.429**‡	44.5 ± 10.57*
Sex (Male: Female)	4:15	3:14	**1.000**†	7:29
Weight (Kg)	72.79 ± 10.97*	69.58 ± 10.52*	**0.379**‡	71.28 ± 10.73*
Height (Metres)	1.58 ± 0.07*	1.56 ± 0.07*	**0.285**‡	1.57 ± 0.07*
Body Mass Index (B.M.I.)	28.90 ± 3.28*	28.59 ± 3.24*	**0.705**‡	28.75 ± 3.22*
Number Of Obese Patients	6/19 (31.58%)	5/17 (29.41%)	**1.000**†	11/36 (30.55%)

* Values are mean ± standard deviation

‡ 2-tailed significance from T-Test for Independent Samples

† 2-sided exact significance from Fischer's Exact Test

The Body Mass Index (B.M.I.) of patients in Group I range from 25.00 to 38.46, the average being 28.90. In Group II, the average B.M.I. is 28.59, with a range extending from 25.15 to 35.43. The surgical procedures performed included thyroidectomies, neck dissections, mastectomies, laparotomies and hernioplasties. The commonest were thyroidectomies and mastectomies.

TABLE 2: INTERVENTION GROUPS

	GROUP I* (6 mL/kg)	GROUP II* (10 mL/kg)	**p Value**†
Tidal Volume (mL)	331.84 ± 31.63	536.76 ± 50.87	**<0.001**

***** Values are mean ± standard deviation

† 2-tailed significance from T-Test for Independent Samples

The patients in the study were randomized to receive either tidal volumes of either 6 mL/kg or 10 mL/kg of ideal body weight (I.B.W.). The difference is shown in **Table 2**. As is evident from the p-Value of <0.001, there is a significant difference in the tidal volumes delivered in the two groups. As there is no statistical difference in other variables (as shown by **Table1**), any significant difference in the outcomes can be reasonably assumed to be due to this difference in intervention.

$ETCO_2$ EXCEEDING DEFINED LIMITS (PRIMARY OUTCOME)

The acceptable $ETCO_2$ limits were set as 24 to 40. If the $ETCO_2$ exceeded these limits, the ventilator settings were changed. The results are given in **Table 3A** and **Table 3B**.

In Group I (6 mL/kg) nearly 74% of patients (14 out of 19 cases) had inadequate ventilation as measured by $ETCO_2$ exceeding the acceptable upper limit of 40 while in Group II (10 mL/kg), only 6% of patients (only 1 out of 17 cases) had inadequate ventilation. This is a statistically significant difference. This is shown in **Table 3A** and **Figure 5**.

TABLE 3A: $ETCO_2$ EXCEEDING UPPER LIMIT OF 40

DID $ETCO_2$ EXCEED 40?	GROUP I (6 mL/kg)	GROUP II (10 mL/kg)	**p Value**
Yes	14/19 (73.7%)	1/17 (5.9%)	**<0.001** (2-sided Exact Significance from Fischer's Exact Test)
No	5/19 (26.3%)	16/17 (94.1%)	

FIG. 5: COMPARISON BETWEEN GROUPS ON PRIMARY OUTCOME

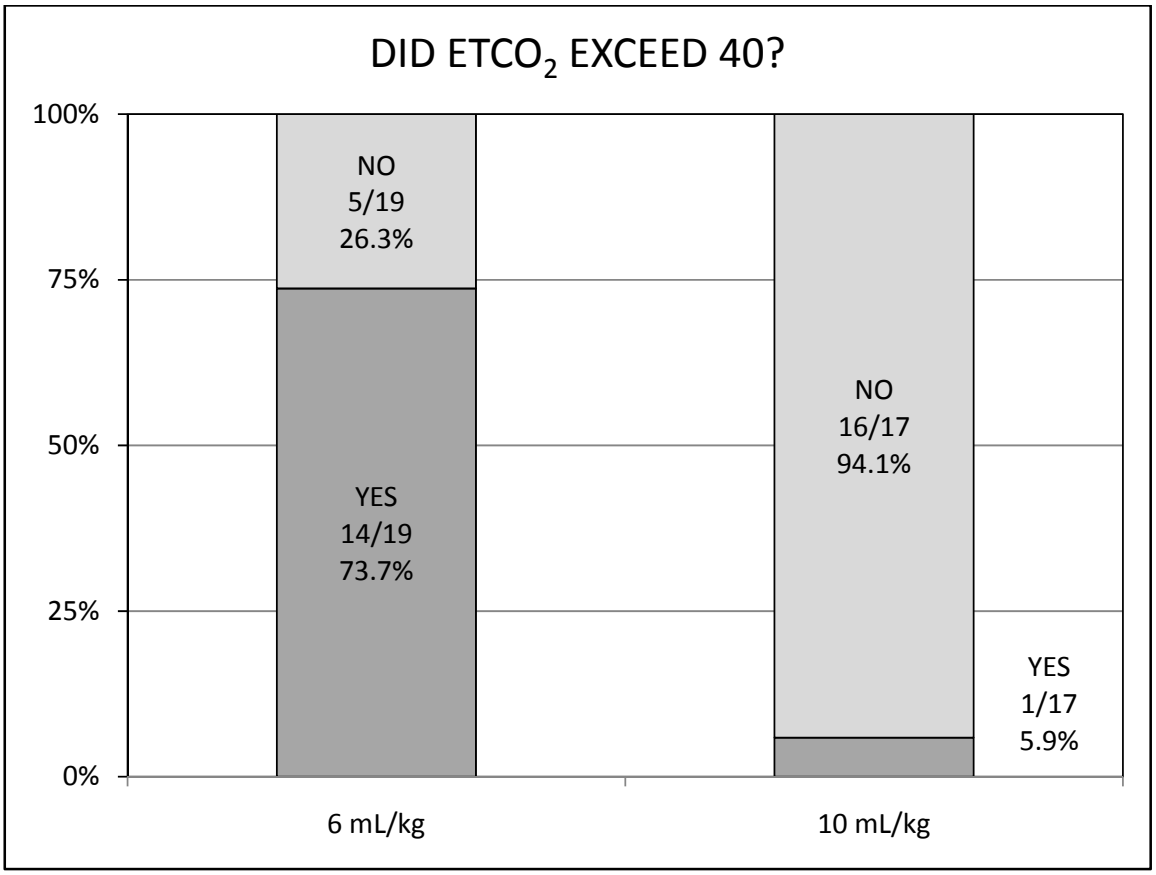


TABLE 3B: $ETCO_2$ DROPPING BELOW LOWER LIMIT OF 24

DID $ETCO_2$ FALL BELOW 24?	GROUP I (6 mL/kg)	GROUP II (10 mL/kg)	**p Value**
Yes	0/19 (0%)	15/17 (88.2%)	**<0.001** (2-sided Exact Significance from Fischer's Exact Test)
No	19/19 (100%)	2/17 (11.8%)	

Table 3B displays the number of cases in each group in which the $ETCO_2$ exceeded the acceptable lower limit of 24. None of the patients in Group I (6 mL/kg) showed an $ETCO_2$ value below 24 at any given time. On the other hand, in Group II (10 mL/kg), there were 15 (out of 17) patients in whom the $ETCO_2$ dropped below 24.

VENTILATOR SETTINGS

Based on the changes in $ETCO_2$, the ventilator settings were changed as specified in the Methodology section. We attempted to derive a possible best tidal volume (per kilogram of ideal or actual body weight) such that, had we started the ventilation with that tidal volume, the $ETCO_2$ would have stayed within the defined limits. The settings at which the $ETCO_2$ stayed within defined limits (24-40) were noted and the final minute ventilation calculated as a product of the tidal volume and respiratory rate.

Final Minute Ventilation (total) =

(Final Tidal Volume) x (Final Respiratory Rate)

Table 4 shows that there was no difference between the two groups in terms of the final minute ventilation needed to maintain the $ETCO_2$ between defined limits.

TABLE 4: FINAL MINUTE VENTILATION

	GROUP I* (6 mL/kg)	GROUP II* (10 mL/kg)	**p Value**†
Final Minute Ventilation (mL/min)	5316.32 ± 605.60	5250 ± 583.35	**0.879**

* Values are mean ± 95% confidence intervals

† 2-tailed significance from T-Test for Independent Samples

The final minute ventilation was divided separately by the ideal body weight and actual body weight to provide the final minute ventilation per kilogram of ideal and actual body weight.

Final Minute Ventilation (per kg IBW) =

$$\frac{\text{Final Minute Ventilation (total)}}{\text{Ideal Body Weight}}$$

Final Minute Ventilation (per kg BW) =

$$\frac{\text{Final Minute Ventilation (total)}}{\text{Actual Body Weight}}$$

These products were finally divided by 12 (assuming 12 breaths per minute) to derive a possible best tidal volume to start with, such that the $ETCO_2$ would have stayed within defined limits from the beginning.

Suggested Tidal Volume (per kg IBW) =

$$\frac{\text{Final Minute Ventilation (per kg IBW)}}{12}$$

Suggested Tidal Volume (per kg Actual BW) =

$$\frac{\text{Final Minute Ventilation (per kg BW)}}{12}$$

TABLE 5: SUGGESTED TIDAL VOLUMES

SUGGESTED TIDAL VOLUME (Assuming Respiratory Rate of 12 breaths per minute)	GROUP I* (6 mL/kg)	GROUP II* (10 mL/kg)	**p Value**†
Based on Ideal Body Weight	8.02 ± 0.89 mL/kg	8.25 ± 1.15 mL/kg	**0.747**
Based on Actual Body Weight	6.11 ± 0.66 mL/kg	6.31 ± 0.63 mL/kg	**0.668**

* Values are mean ± 95% confidence intervals

† 2-tailed significance from T-Test for Independent Samples

The results are given in **Table 5**. In both groups, the suggested tidal volume is about 8 mL/kg of ideal body weight (7-9 mL/kg taking the 95% confidence intervals into consideration). There is no significant difference in the suggested tidal volumes between the two groups.

ARTERIAL BLOOD GAS VARIABLES

Arterial blood samples were drawn for analysis at the beginning (sample A) of controlled ventilation and two hours after the first sample (sample B). The means with confidence intervals for the variables are given in **Table 6A** and **Table 6B**.

TABLE 6A: A.B.G. ANALYSIS FOR GROUP I (6 mL/kg)

VARIABLE	SAMPLE A*	SAMPLE B*	**p Value†**
pH	7.36 ± 0.02	7.32 ± 0.03	**<0.001**
P_aO_2 (mm Hg)	204.84 ± 26.27	168.57 ± 24.90	**0.016**
P_aCO_2 (mm Hg)	45.50 ± 1.65	47.60 ± 2.47	**0.129**
HCO_3^- (mMol/L)	25.66 ± 1.62	24.16 ± 1.54	**0.001**
Base Excess (mMol/L)	0.65 ± 1.70	-1.33 ± 1.64	**0.001**
S_aO_2 (%)	99.31 ± 0.42	98.69 ± 0.76	**0.168**

* Values are mean ± 95% confidence intervals

† 2-tailed significance from T-Test for Paired Samples

In **Table 6A**, the comparison between Sample A and Sample B for the patients in Group I is shown. As can be seen, there was a significant drop in the pH and oxygenation at the end of two hours of low tidal volume ventilation. There was also a rise in the P_aCO_2 at the end of two hours but it was not significant.

In **Table 6B**, the comparison between Sample A and Sample B for the patients in Group II is shown. As can be seen, there was no change in the pH and oxygenation at the end of two hours of conventional tidal volume ventilation but there was a significant drop in the P_aCO_2.

In **Table 6A** and **Table 6B**, there seems to be a statistically significant difference in HCO_3^- concentration and Base Excess between Sample A and Sample B in both low and

TABLE 6B: A.B.G. ANALYSIS FOR GROUP II (10 mL/kg)

VARIABLE	SAMPLE A*	SAMPLE B*	**p Value†**
pH	7.42 ± 0.02	7.41 ± 0.03	**0.400**
P_aO_2 (mm Hg)	231.38 ± 34.85	237.06 ± 24.28	**0.733**
P_aCO_2 (mm Hg)	38.54 ± 3.43	35.86 ± 2.23	**0.026**
HCO_3^- (mMol/L)	25.01 ± 1.19	23.36 ± 0.97	**0.001**
Base Excess (mMol/L)	0.09 ± 1.12	-1.75 ± 1.07	**<0.001**
S_aO_2 (%)	99.21 ± 1.03	99.74 ± 0.19	**0.297**

* Values are mean ± 95% confidence intervals

† 2-tailed significance from T-Test for Paired Samples

conventional tidal volume groups. However, the means and confidence intervals lie within the clinically normal range and the change is minimal in actual terms and does not represent any metabolic acid-base abnormality.

The inter-group comparisons of sample A and sample B are given in **Table 6C** and **Table 6D**. Sample A (**Table 6C**) was taken as soon as possible after putting the patient on the ventilator. There seems to have been a rapid effect on the pH and P_aCO_2 which were statistically different between the two groups. However, there was no difference in P_aO_2 between the two groups. The possible explanation for the difference in pH and P_aCO_2 will be discussed later.

Sample B was taken two hours after sample A in both the low tidal volume and

TABLE 6C: FIRST ARTERIAL BLOOD GAS ANALYSIS (SAMPLE A)

VARIABLE	GROUP I* (6 mL/kg)	GROUP II* (10 mL/kg)	**p Value†**
pH	7.36 ± 0.02	7.42 ± 0.02	**0.003**
P_aO_2 (mm Hg)	204.84 ± 26.27	231.38 ± 34.85	**0.236**
P_aCO_2 (mm Hg)	45.50 ± 1.65	38.54 ± 3.43	**0.001**
HCO_3^- (mMol/L)	25.66 ± 1.62	25.01 ± 1.19	**0.537**
Base Excess (mMol/L)	0.65 ± 1.70	0.09 ± 1.12	**0.600**
S_aO_2 (%)	99.31 ± 0.42	99.21 ± 1.03	**0.865**

* Values are mean ± 95% confidence intervals

† 2-tailed significa2nce from T-Test for Independent Samples

TABLE 6D: SECOND ARTERIAL BLOOD GAS ANALYSIS (SAMPLE B)

VARIABLE	GROUP I* (6 mL/kg)	GROUP II* (10 mL/kg)	**p Value†**
pH	7.32 ± 0.03	7.41 ± 0.03	**<0.001**
P_aO_2 (mm Hg)	168.57 ± 24.90	237.06 ± 24.28	**0.001**
P_aCO_2 (mm Hg)	47.60 ± 2.47	35.86 ± 2.23	**<0.001**
HCO_3^- (mMol/L)	24.16 ± 1.54	23.36 ± 0.97	**0.408**
Base Excess (mMol/L)	-1.33 ± 1.64	-1.75 ± 1.07	**0.684**
S_aO_2 (%)	98.69 ± 0.76	99.74 ± 0.19	**0.017**

* Values are mean ± 95% confidence intervals

† 2-tailed significance from T-Test for Independent Samples

conventional tidal volume groups. As shown in **Table 6D**, there was a significant drop in pH and P_aO_2, and a significant rise in the P_aCO_2 in the low tidal volume group. There was also a statistically significant but clinically non-significant difference in S_aO_2 between the two groups.

RESPIRATORY ACIDOSIS OR ALKALOSIS (SECONDARY OUTCOME)

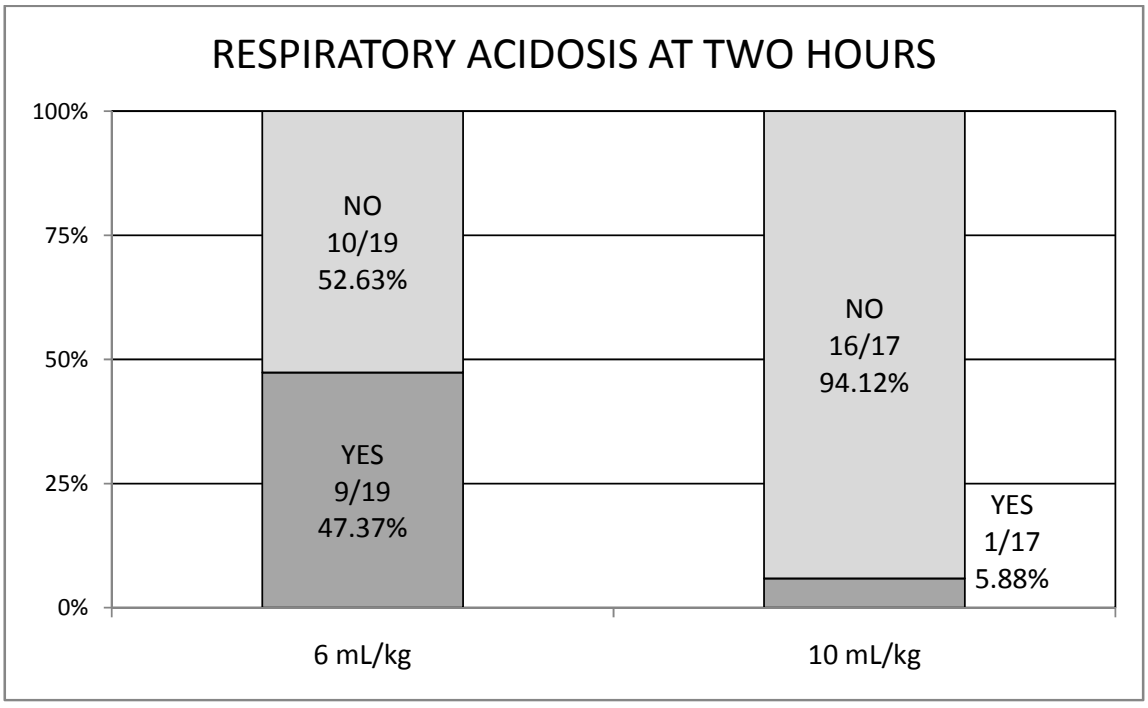
The limits for acceptable pH were defined as being from 7.35 to 7.45(9)(7). Based on the presence of an abnormal pH with a corresponding change in the P_aCO_2 outside the normal range of 35 to 45 mm Hg, the results are given in **Table 7A** and **Table 7B**.

TABLE 7A: RESPIRATORY ACIDIOSIS

	GROUP I (6 mL/kg)	GROUP II (10 mL/kg)	**p Value*** (difference between Group I and Group II)
SAMPLE A	3/19 (15.79%)	1/17 (5.88%)	**0.605**
SAMPLE B	9/19 (47.37%)	1/17 (5.88%)	**0.008**
p Value* (difference between Sample A and Sample B)	**0.079**	**1.000**	

* 2-sided Exact Significance from Fischer's Exact Test

FIG. 6: COMPARISON BETWEEN GROUPS ON SECONDARY OUTCOME



Respiratory acidosis is considered in **Table 7A**. There is no significant difference between the two groups at the beginning (sample A). However, at the end of two hours (sample B), 47% of patients in Group I (6 mL/kg) had respiratory acidosis as compared to only 6% of cases in Group II (10 mL/kg) which is a statistically significant difference as shown in **Figure 6**.

Furthermore, 6 patients out of 19 (about one third) in Group I (6 mL/kg) ended up developing respiratory acidosis during the two hours of low tidal volume ventilation while no additional patients developed respiratory acidosis in Group II (10 mL/kg). This difference was tending towards statistical significance (p = 0.079).

TABLE 7B: RESPIRATORY ALKALOSIS

	GROUP I (6 mL/kg)	GROUP II (10 mL/kg)	**p Value*** (difference between Group I and Group II)
SAMPLE A	0/19 (0%)	4/17 (23.53%)	**0.040**
SAMPLE B	0/19 (0%)	3/17 (17.65%)	**0.095**
p Value* (difference between Sample A and Sample B)	**Not Applicable**	**1.000**	
* 2-sided Exact Significance from Fischer's Exact Test			

Table 7B displays the results on development of respiratory alkalosis. About one-fifth of the patients in Group II (10 mL/kg) showed respiratory alkalosis in both sample A and sample B while none of the patients in Group I (6mL/kg) had respiratory alkalosis in either arterial blood sample. The difference between the two groups in terms of presence of respiratory alkalosis is statistically significant in the beginning (sample A) and tending towards statistical significance at the end of two hours (sample B).

INDICES OF OXYGENATION

The alveolar-arterial oxygen gradient (A-a Gradient: difference between P_AO_2 and P_aO_2) and the PaO_2-F_iO_2 ratio (P/F Ratio: PaO_2 divided by F_iO_2) for each arterial blood sample were calculated. Because of the large standard deviations and confidence intervals, we suspected that the data may not follow a normal distribution. We performed the Kolmogorov-Smirnov test of normality for the data which showed that the distribution of some of the variables was significantly different from a normal distribution. Under the circumstances, non-parametric tests are a better choice for analysing significant differences. The results are displayed in **Table 8A** and **Table 8B**.

The difference between the two groups is highlighted in **Table 8A**. There is no statistical difference in alveolar-arterial oxygen gradient or PaO_2-F_iO_2 ratio between the two groups in the beginning but at the end of two hours of ventilation with low or conventional tidal volumes, there is a significant rise in the alveolar-arterial oxygen gradient and a significant drop in the PaO_2-F_iO_2 ratio in the low tidal volume group.

TABLE 8A: OXYGENATION INDICES (COMPARING GROUP I & GROUP II)

VARIABLE	GROUP I* (6 mL/kg)	GROUP II* (10 mL/kg)	**p Value†**
SAMPLE A			
A-a Gradient	172.91 ± 25.90	154.02 ± 33.18	**0.366**
P/F Ratio	341.40 ± 43.79	385.65 ± 58.08	**0.267**
SAMPLE B			
A-a Gradient	206.87 ± 25.05	151.30 ± 23.09	**0.004**
P/F Ratio	280.95 ± 41.51	395.10 ± 40.46	**0.001**

* Values are mean ± 95% confidence intervals

† 2-tailed significance from Mann-Whitney test

TABLE 8B: OXYGENATION INDICES (COMPARING SAMPLE A & SAMPLE B)

VARIABLE	SAMPLE A*	SAMPLE B*	**p Value†**
GROUP I (6 mL/kg)			
A-a Gradient	172.91 ± 25.90	206.87 ± 25.05	**0.016**
P/F Ratio	341.40 ± 43.79	280.95 ± 41.51	**0.011**
GROUP II (10 mL/kg)			
A-a Gradient	154.02 ± 33.18	151.30 ± 23.09	**0.653**
P/F Ratio	385.65 ± 58.08	395.10 ± 40.46	**0.421**

* Values are mean ± 95% confidence intervals

† 2-tailed significance from Wilcoxon Signed Ranks test

The Wilcoxon Signed Ranks test for paired samples displays the same results comparing variables at the beginning and end of the intervention. This is displayed in **Table 8B** where there is no difference in oxygenation indices in Group II between sample A and sample B but a significant difference between the two samples in the low tidal volumes group (Group I). This difference is also shown in **Figure 7** and **Figure 8**. It is noteworthy that in the low tidal volume group, the P/F Ratio after two hours of ventilation drops below 300, which is clinically significant.

FIG.7: COMPARISON OF ALVEOLAR-ARTERIAL OXYGEN GRADIENTS

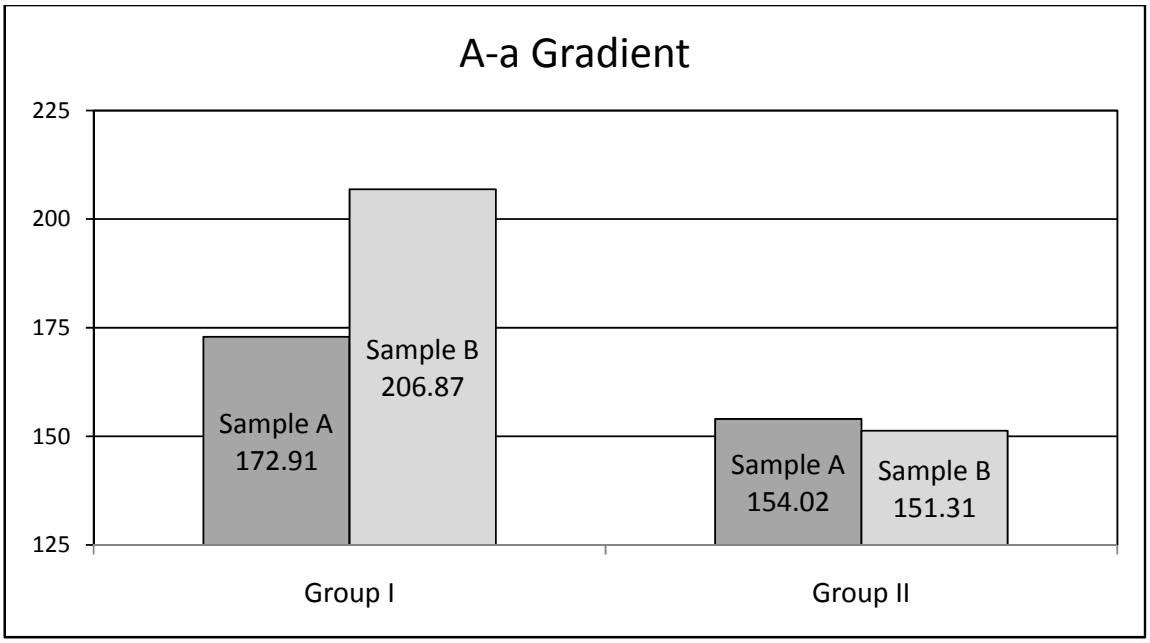
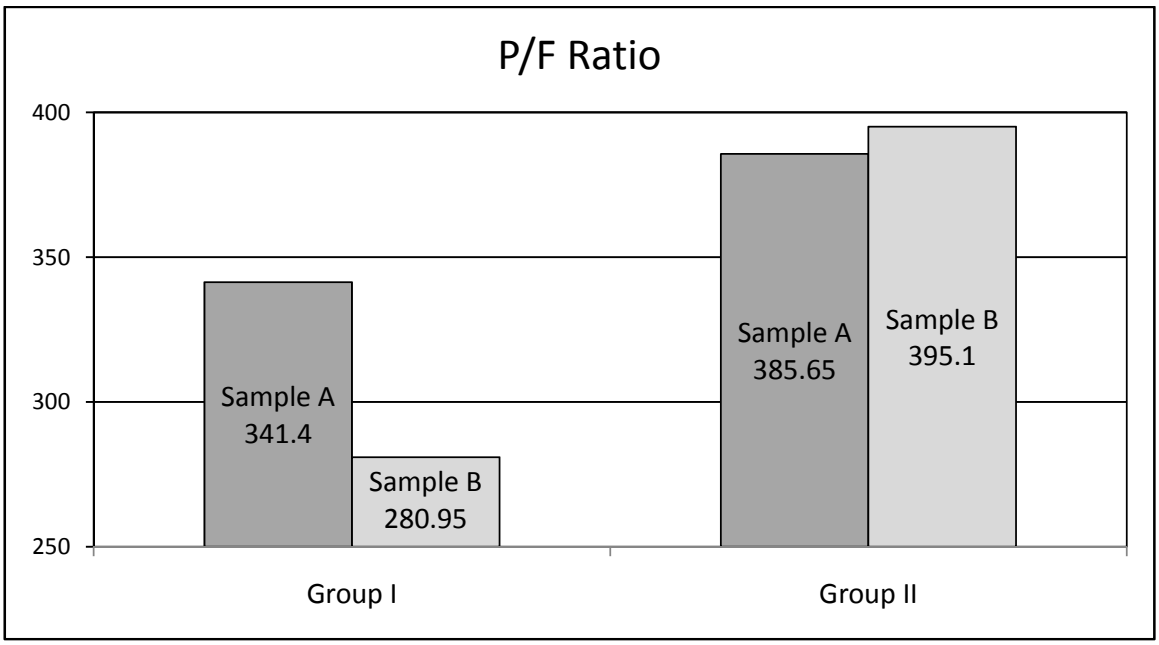


FIG.8: COMPARISON OF P_aO_2-F_iO_2 RATIO



CHANGE IN INDICES OF OXYGENATION (SECONDARY OUTCOME)

The changes in alveolar-arterial oxygen gradient and P_aO_2-F_iO_2 ratio from Sample A to Sample B were analysed in all patients. Again, a non-parametric test (the Mann-Whitney test) was performed to assess for significant differences between the two groups. The results are given in **Table 9**. There is hardly any change in the alveolar-arterial oxygen gradient and P_aO_2-F_iO_2 ratio in the conventional tidal volume group (Group II) while there is a significant rise in the alveolar-arterial oxygen gradient and significant drop in the P_aO_2-F_iO_2 over two hours of low tidal volume ventilation (Group I). This is displayed in **Figure 9** and **Figure 10**.

TABLE 9: CHANGE IN INDICES OF OXYGENATION

	GROUP I* (6 mL/kg)	GROUP II* (10 mL/kg)	**p Value†**
A-a Gradient Difference (Sample B - Sample A)	+33.96 (± 26.81)	-2.73 (± 32.08)	**0.018**
P/F Ratio Difference (Sample B – Sample A)	-60.46 (± 44.65)	+9.59 (± 53.32)	**0.012**

* Values are mean (± 95% confidence intervals)

† 2-tailed significance from Mann-Whitney test

FIG. 9: CHANGE IN ALVEOLAR-ARTERIAL OXYGEN GRADIENT

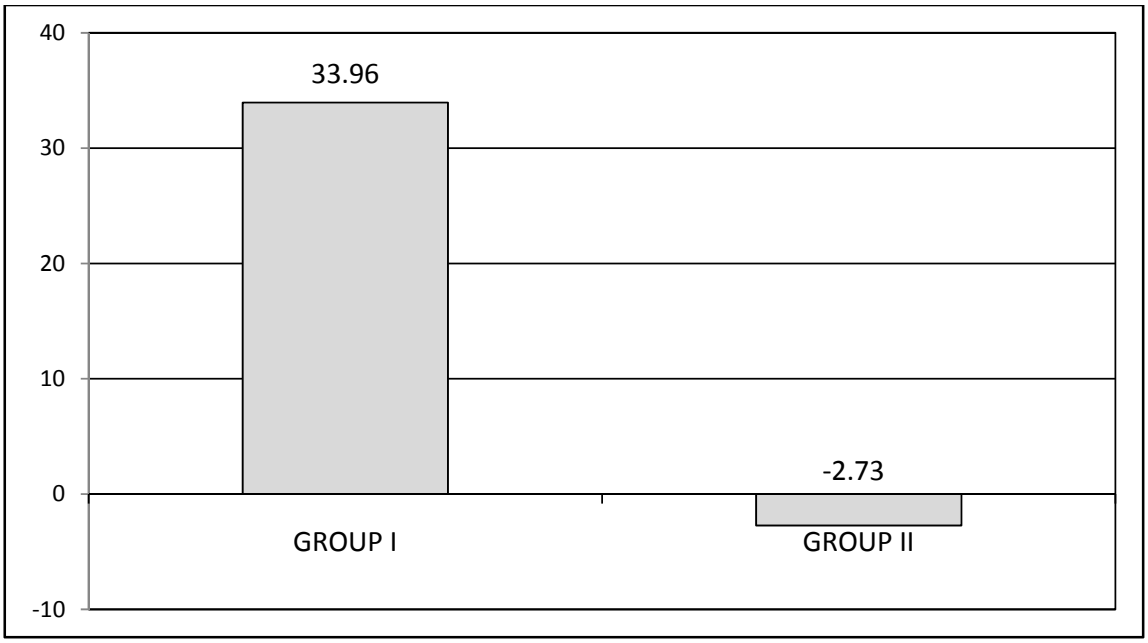
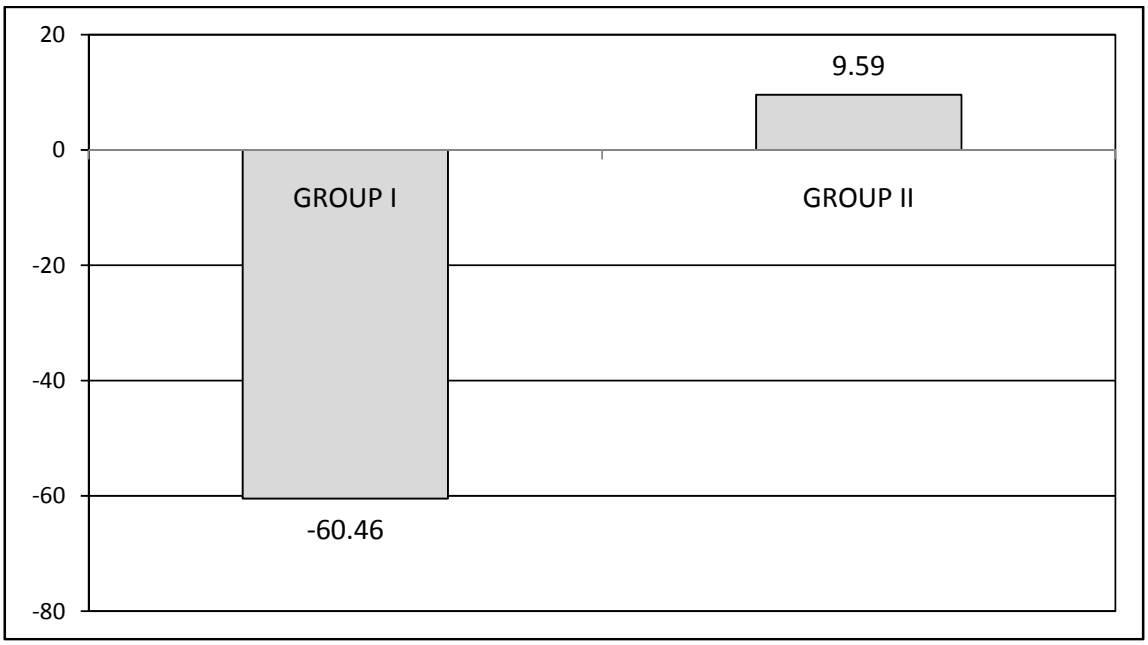


FIG. 10: CHANGE IN P_aO_2-F_iO_2 RATIO



CHANGE IN P_aCO_2-$ETCO_2$ GRADIENT (SECONDARY OUTCOME)

The change in P_aCO_2-$ETCO_2$ gradient from Sample A to Sample B was calculated for each patient. The results are given in **Table 10**. As shown, there is no significant difference between the changes in P_aCO_2-$ETCO_2$ gradient between the two groups. However, the gradient is more in the low tidal volume group in both samples (the difference is statistically significant in sample B).

TABLE 10: CHANGE IN P_aCO_2-$ETCO_2$ GRADIENT

P_aCO_2-$ETCO_2$ gradient	GROUP I* (6 mL/kg)	GROUP II* (10 mL/kg)	**p Value†**
Sample A	12.24 ± 2.24	9.59 ± 2.47	**0.136**
Sample B	11.71 ± 1.96	8.51 ± 1.47	**0.031**
Change in Gradient (Sample B - Sample A)	-0.53 (± 2.14)	-1.09 (± 1.81)	**0.874**

* Values are mean (± 95% confidence intervals)

† 2-tailed significance from Mann-Whitney test

DISCUSSION

This study compares two different tidal volumes of 6 mL/kg of ideal body weight and 10 mL/kg of ideal body weight during controlled ventilation under general anaesthesia. Traditionally, tidal volumes of 10 mL/kg have been used. Even greater tidal volumes of upto 15 mL/kg are commonly recommended. It must be remembered that resting tidal volumes in normal adults is actually around 7-8 mL/kg. Supra-physiological volumes of 10 mL/kg or more were recommended to counter the near-universal reduction in Functional Residual Capacity (F.R.C.) seen under general anaesthesia.

However, interest in lower tidal volumes was kindled by observations that conventional tidal volumes resulted in exacerbation of lung injury and longer periods of ventilatory support in patients with pre-existing lung injury. Studies have gone on to prove that lower tidal volumes definitely reduce morbidity, mortality and duration of mechanical ventilation in patients with Acute Lung Injury (A.L.I.) and Acute Respiratory Distress Syndrome (A.R.D.S.). As a result, the use of lower tidal volumes is increasing, and this usage is spilling over into the peri-operative setting.

This study attempts to evaluate the effects of low tidal volume ventilation in patients with normal lung function. We hypothesized that low tidal volumes would be ineffective in adequately washing out carbon dioxide (CO_2) and that there would be a need to raise the

minute ventilation by raising the respiratory rate, and perhaps, even the tidal volume. We further hypothesized that there would be a drop in oxygenation with low tidal volume ventilation as compared to conventional tidal volumes based on the fact that low tidal volume is one of the risk factors for atelectasis under mechanical ventilation. Also, we suspected that these effects would be greater in patients with higher body mass index (B.M.I.). Accordingly, we devised a protocol to test our hypothesis.

DEMOGRAPHIC VARIABLES & INTERVENTION

The various demographic variables- age, sex, weight, height, body mass index- were equally distributed in the two groups. The intervention in Group I was a low tidal volume of 6 mL/kg of ideal body weight and the intervention in Group II was a conventional tidal volume of 10 mL/kg of ideal body weight. Statistical analysis shows that the tidal volumes delivered in the two groups were significantly different from each other. In the absence of differences in the other variables, it is reasonable to assume that the differences in outcome between the two groups are a result of the difference in intervention.

$ETCO_2$ EXCEEDING DEFINED LIMITS (PRIMARY OUTCOME)

With regard to the primary outcome, there was a significant difference between the two groups. Using a uniform respiratory rate of 12 breaths per minute, 74% of patients in Group I (6 mL/kg) and only 6% of patients in Group II (10 mL/kg) had inadequate ventilation ($p < 0.001$) as defined by $ETCO_2$ exceeding the upper limit of 40.

On the other hand, almost 90% of patients in Group II (10 mL/kg) had $ETCO_2$ dropping below the lower limit of 24 while none of the patients in Group I (6 mL/kg) had this

occurrence. However, the P_aCO_2 remained within the normal limits. This was taken as evidence of excess ventilation and the minute ventilation was accordingly reduced.

Any concerns about the lower limit of $ETCO_2$ chosen (i.e. 24) being too low should be allayed by the observation that the P_aCO_2 attained with this limit was within the normal range. As displayed in the results table on arterial blood gas variables, the mean P_aCO_2 at the end of two hours of conventional ventilation was 35.86 ± 2.23 mm Hg and the incidence of respiratory alkalosis was not significantly greater in this group. The incidence of hypercapnia and respiratory acidosis in Group I (6 mL/kg) by accepting 40 as the upper limit of $ETCO_2$ were much more than the incidence of hypocapnia and respiratory alkalosis in Group II (10 mL/kg) by accepting 24 as the lower limit of $ETCO_2$.

VENTILATOR SETTINGS

All ventilator variables except the tidal volume were kept uniform at the beginning of mechanical ventilation. As and when the $ETCO_2$ exceeded the defined limits, the respiratory rate was initially changed to a maximum of 18 breaths per minute and a minimum of 6 breaths per minute keeping the tidal volume constant. If the $ETCO_2$ still remained outside the acceptable limits, the tidal volume was changed by 50 mL at a time to attain an acceptable $ETCO_2$. Out of the 14 patients (out of 19; 74%) in Group I (6 mL/kg) whose $ETCO_2$ exceeded 40, 5 patients required an increase in tidal volume (after raising the respiratory rate to 18 breaths per minute) to bring the $ETCO_2$ back to 40 or below.

An assessment of the final minute ventilation needed to maintain $ETCO_2$ within acceptable limits showed no difference between the two groups (5316.32 ± 605.60 mL/min v/s 5250 ± 583.35 mL/min; p = 0.879).

From the final minute ventilation needed, we attempted to derive a suggested tidal volume such that had the mechanical ventilation been started with that tidal volume (keeping all other parameters unchanged including respiratory rate of 12 breaths per minute), the $ETCO_2$ would have remained within acceptable limits. This tidal volume turned out to be 8.02 ± 0.89 mL/kg of ideal body weight in Group I (6 mL/kg) and 8.25 ± 1.15 mL/kg of ideal body weight in Group II (10 mL/kg) and there was no significant difference ($p = 0.747$) between the two groups in this regard.

It is interesting to note that this suggested tidal volume is very similar to the resting physiological tidal volume. However, it should be remembered that this suggested tidal volume is only calculated with regard to adequate carbon dioxide excretion. The effect of tidal volumes of 8 mL/kg of ideal body weight on the oxygenation parameters cannot be definitely commented upon but may lie somewhere between the oxygenation achieved with low and conventional tidal volumes.

ARTERIAL BLOOD GAS VARIABLES

Sample A was taken as soon as possible after connecting the patient to the ventilator. As such, there should be no difference between the arterial blood gas variables between the two groups because the intervention has just been set in motion. It is known that nearly 90% of all patients develop atelectasis under general anaesthesia and that most of this atelectasis occurs at induction. The effects of this atelectasis should be present equally in both groups.

In practical terms, the delay between connecting the patient to the ventilator and collecting sample A was about 3-5 minutes. This delay may account for the significant difference in P_aCO_2 between the two groups (45.50 ± 1.65 mm Hg v/s 38.54 ± 3.43 mm Hg;

p = 0.001). There is a corresponding significant difference in pH between the two groups. However, the values are within clinically normal limits at the beginning.

Sample B was taken two hours after sample A. This showed a significant difference between the groups in terms of pH, P_aO_2 and P_aCO_2. In the low tidal volume group, the mean P_aCO_2 was in the hypercapnoeic range (47.60 ± 2.47 v/s 35.86 ± 2.23; $p < 0.001$), the mean pH was acidotic (7.32 ± 0.03 v/s 7.41 ± 0.03; $p < 0.001$) and the mean P_aO_2 was significantly lower than in the conventional tidal volume group (168.57 ± 24.90 v/s 237.06 ± 24.28; p = 0.001).

In a study by Cai et al(26), 16 patients with normal lung function and B.M.I. less than 25 undergoing craniotomy were ventilated with tidal volumes of 6 mL/kg or 10 mL/kg (8 subjects in each group). They found no significant difference in P_aCO_2 between the two groups at the beginning, as well as at the end.

In a study by Tweed et al(25), 24 adults undergoing gynaecological surgeries were ventilated with either 7.5 mL/kg or 12.5 mL/kg tidal volumes. They too did not find any significant differences in P_aCO_2 between the two groups. Our findings are different from the findings in these two trials with regard to P_aCO_2.

RESPIRATORY ACIDOSIS OR ALKALOSIS (SECONDARY OUTCOME)

Based on the normal values of pH and P_aCO_2, a patient was deemed to have respiratory acidosis if the pH was below 7.35 and the P_aCO_2 above 45, while the patient was deemed to have respiratory alkalosis if the pH was above 7.45 and the P_aCO_2 below 35. Based on these definitions, 47% of patients in Group I (6 mL/kg) had respiratory acidosis at the end of two

hours while only 6% of patients in Group II (10 mL/kg) had respiratory acidosis. This difference was significant (p = 0.008).

While none of the patients in Group I (6 mL/kg) developed respiratory alkalosis, 3 out of 17 patients in Group II (10 mL/kg) had respiratory alkalosis at the end of two hours.

CHANGE IN INDICES OF OXYGENATION (SECONDARY OUTCOME)

Alveolar-arterial oxygen gradient (A-a Gradient) and P_aO_2- F_iO_2 Ratio (P/F Ratio) were calculated for all the arterial blood samples. There was no significant difference between the two variables at the beginning. At the end of two hours, there was hardly any change in the variables in the conventional tidal volume group but there was a significant worsening of oxygenation indices in the low tidal volume group. The A-a Gradient increased [+33.96 (± 26.81) v/s -2.73 (± 32.08); p = 0.018] whereas the P/F Ratio decreased [-60.46 (± 44.65) v/s +9.59 (± 53.32); p = 0.012].

Cai et al(26), in their study, found no difference between 6 mL/kg and 10 mL/kg tidal volumes in terms of A-a Gradient or P/F Ratio. A closer look at their data shows that the mean A-a Gradient was higher and the mean P/F Ratio lower in the 6 mL/kg group than in the 10 mL/kg. The values did not attain statistical significance, perhaps because of the small sample size.

In the study by Tweed et al(25), similar findings were noted. While the mean A-a Gradient was higher in the 7.5 mL/kg tidal volume group than in the 12.5 mL/kg tidal volume group, the values did not attain statistical significance.

CHANGE IN P_aCO_2-$ETCO_2$ GRADIENT (SECONDARY OUTCOME)

There was no significant difference between the two groups in terms of change in the P_aCO_2-$ETCO_2$ gradient. This can be explained by the fact that the P_aCO_2-$ETCO_2$ gradient depends on the amount of dead space, as opposed to the A-a Gradient which depends on the amount of shunt. In the absence of P.E.E.P., the dead space in the two groups can be assumed to be similar, resulting in similar P_aCO_2-$ETCO_2$ gradients.

OBESE PATIENTS

The number of obese patients in the study was small (6/19 in Group I and 5/17 in Group II). A statistical analysis on the obese patients alone showed no difference between low and conventional tidal volume ventilation in terms of indices of oxygenation. In the obese patients, the mean A-a Gradient increased and the mean P/F Ratio decreased even in the conventional tidal volume group. This may suggest that even tidal volumes of 10 mL/kg of ideal body weight are inadequate in obese patients. If that is the case, they may require higher tidal volumes of upto 15 mL/kg or addition of P.E.E.P. to improve oxygenation. However, it is also possible that the non-significant results attained when comparing the two tidal volumes within the sub-group of obese patients are due to the small sample size.

LIMITATIONS

1. P.E.E.P.: The effect of Positive End-Expiratory Pressure has not been assessed in this study. P.E.E.P. is not used very commonly for controlled ventilation under anaesthesia unless patients are already being ventilated in a critical care set-up for lung injury. This is probably because of its adverse effects on cardiac output, systemic oxygen delivery and intra-cranial pressure, and the propensity to increase venous bleeding during surgery in certain vascular tissue like the liver and brain. It is possible that the use of P.E.E.P. may improve oxygenation in both groups. However, the quantity of the effect in the two groups may not be similar.
2. Obesity: The number of obese patients in the study (11 out of 36) was too low to assess the effect of the two ventilation strategies separately in them. However, they were equally distributed in the two groups.
3. Upper Abdominal Procedures: While it is known that packing and retraction during upper abdominal procedures may increase the amount of atelectasis, it is unknown whether this effect is significant during controlled ventilation with fixed tidal volumes. Theoretically, tidal volumes set on the ventilator should be achievable even with such atelectasis. In our study, we have included patients undergoing upper abdominal surgeries also.

CONCLUSIONS

In this study comparing the adequacy of ventilation with tidal volumes of 6 mL/kg and 10 mL/kg of ideal body weight in overweight and obese patients, we reached the following conclusions:

1. Patients in the low tidal volume group had a significantly greater incidence (73.7% v/s 5.9%; $p < 0.001$) of inadequate ventilation as measured by the need to raise respiratory rate with or without additional increases in the tidal volume to maintain $ETCO_2$ within acceptable limits. At the same time, a significantly greater number of patients in the conventional tidal volume group (88.2% v/s 0%; $p < 0.001$) needed a reduction in respiratory rate with or without additional decreases in the tidal volume to prevent the $ETCO_2$ from dropping too low.
2. There was a significantly greater incidence of respiratory acidosis in the low tidal volume group than in the conventional tidal volume group (47.4% v/s 5.9%; $p = 0.008$) at the end of two hours.
3. Low tidal volume ventilation resulted in a significant worsening (increase) in the alveolar-arterial oxygen gradient at the end of two hours while there was no change in the conventional tidal volume group ($+33.96 \pm 26.81$ v/s -2.73 ± 32.08; $p = 0.018$).

4. Patients in the low tidal volume ventilation group had a significant worsening (decrease) of the P/F Ratio at the end of two hours while there was no change in the conventional tidal volume group (-60.46 ± 44.65 v/s +9.59 ± 53.32; p = 0.012).
5. No significant difference between the two groups was found in the change in P_aCO_2-$ETCO_2$ gradient (-0.53 ± 2.14 v/s -1.09 ± 1.81; p = 0.874)

To summarize, **low tidal volume ventilation results in significantly greater incidences of inadequate ventilation and respiratory acidosis and significant worsening of oxygenation as compared to conventional tidal volume ventilation in overweight and obese patients**.

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11. APPENDIX

A. Thesis Protocol Sheet

B. Data Collection Sheet

C. Patient Information Sheet

D. Consent Form

E. Data Spread Sheet

APPENDIX A: THESIS PROTOCOL SHEET

COMPARING LOW AND NORMAL TIDAL VOLUMES DURING INTERMITTENT POSITIVE PRESSUE VENTILATION

INCLUSION AND EXCLUSION CRITERIA

INCLUSION CRITERIA:

A.S.A. physical status 1 and 2 adult patients with normal respiratory function and a B.M.I. of 25 or more undergoing elective general surgical procedures under general anaesthesia with I.P.P.V.

EXCLUSION CRITERIA:

1) A.S.A. physical status 3 and 4 patients;
2) Patients aged less than 18 years or more than 75 years;
3) B.M.I. of less than 25;
4) Patients with known respiratory disorders (except Obstructive Sleep Apnoea);
5) Smoking history of 20 pack years or more;
6) Patients with pre-existing acid-base abnormalities;
7) Emergency procedures;
8) Laparoscopic procedures;
9) Procedures involving thoracotomy or alteration of ventilatory parameters for surgical purposes;
10) Procedures taking less than 2 hours duration;
11) Known allergic reaction to any of the specified drugs;
12) Refusal/ inability to give consent.

PROTOCOL

PRE-OPERATIVE STEPS:

Once inclusion and exclusion criteria have been satisfied,

1) Informed consent is taken;
2) Height is measured in metres;
3) Ideal body weight is calculated using the formula:

$$I.B.W. = 22 \times [\text{Height (in metres)}]^2$$

4) Tidal volumes at 6 mL/kg and at 10 mL/kg of I.B.W. are calculated and noted;

STEPS IN OPERATING THEATRE:

1) Intra-venous access is obtained;
2) Monitoring is established as indicated for the case;
3) CO_2 analyzer/ gas analyzer calibration and functioning is confirmed;
4) Drugs for induction and maintenance are as per the care-giver's decision;
5) After endo-tracheal intubation, the patient is connected to the ventilator with the following settings:

   Volume-Control ventilation,
   Tidal Volume- as per randomization (6 mL/kg or 10 mL/kg),

   Rate- 12 breaths per minute,

   P.E.E.P.- 0 cm H_2O,

   I:E Ratio- 1:2,

   Inspiratory Pressure Limit- 35 cm H_2O.

6) F_iO_2 is set at 0.6. (60%)
7) Immediately after connecting to the ventilator, an A.B.G. sample is obtained from a radial artery puncture using a 26 gauge needle after flushing the syringe with heparinised saline;
8) $ETCO_2$ and F_iO_2 are noted at the time of obtaining ABG sample;
9) Adequate compression is provided for the radial artery puncture site;
10) The radial artery is examined intermittently intra-operatively to assess for pulsation, bleeding, and development of any haematoma;
11) $ETCO_2$ is monitored throughout the procedure. If it exceeds 40 cm H_2O at any time, the respiratory rate is increased by 2 breaths per minute at a time till the $ETCO_2$ is brought back to or under 40 cm H_2O. If the $ETCO_2$ falls below 24 cm H_2O at any time, the respiratory rate is reduced by 2 breaths per minute at a time till the $ETCO_2$ is brought back to or above 24 cm H_2O.
12) The need to change the respiratory rate is noted along with the time since first A.B.G.
13) If $ETCO_2$ remains above 40 cm H_2O despite a respiratory rate of 18 breaths per minute, the tidal volume is increased in increments of 50 mL as needed to bring the $ETCO_2$ back to or below 40 cm H_2O. The need to change the tidal volume is noted.
14) If $ETCO_2$ remains below 24 cm H_2O despite a respiratory rate of 6 breaths per minute, the tidal volume is reduced by decrements of 50 mL as needed to bring back the $ETCO_2$ to or above 24 cm H_2O. The need to change the tidal volume is noted.
15) 2 hours after the first A.B.G., a second A.B.G. sample is drawn in a similar manner to the first one, and $ETCO_2$ and F_iO_2 are noted at the time of obtaining the sample.
16) Adequate compression is provided to the radial artery puncture site and a tight occlusive dressing is placed over the site.
17) Any respiratory acid-base abnormality detected on the second A.B.G. is treated as necessary.
18) After the second A.B.G. is collected, the ventilator settings can be re-adjusted as deemed necessary by the care-giver.

CALCULATIONS

P_aCO_2-$ETCO_2$ gradient = $P_aCO_2 - ETCO_2$

where: P_aCO_2 is measured from the A.B.G. sample;

$ETCO_2$ is monitored by the CO2 analyzer/ gas analyzer.

$P_AO_2 = [F_iO_2 \times (760 - 47)] - [P_ACO_2/R] + [P_ACO_2 \times F_iO_2 \times \{(1 - R)/R\}]$

where: FiO2 is as per the fresh-gas flow settings;

P_ACO_2 (alveolar) = P_aCO_2 (with normal respiratory function);

R(respiratory quotient) = 0.8 (under normal conditions).

P_AO_2-P_aO_2 gradient= $P_AO_2 - P_aO_2$

where: P_aO_2 is measured from the A.B.G. sample.

P_aO_2- F_iO_2 ratio= P_aO_2 / F_iO_2

where: P_aO_2 is measured from the A.B.G. sample;

FiO2 is as per the fresh-gas flow settings.

APPENDIX B: DATA COLLECTION SHEET

COMPARING LOW AND NORMAL TIDAL VOLUMES DURING INTERMITTENT POSITIVE PRESSUE VENTILATION

PRE-OPERATIVE

Name: Age: (yrs) Sex: M/F

Hospital No.:

Weight: (kg)

Height: (m) [1 m= 100 cm, 1 inch = 2.5 cm, I foot = 12 inches]

B.M.I.: [(weight in kilograms)/(height in metres)^2]

Ideal Body Weight (I.B.W.): (kg) [22 x (height in metres)^2]

Procedure:

Tidal volume: Low (mL) [6 mL/ kg of I.B.W.]

Normal (mL) [10 mL/ kg of I.B.W.]

(Rounded off to the nearest 25 mL)

INSIDE OPERATING THEATRE

Initial Ventilator Settings: Time of Setting Ventilator:

Tidal Volume: (mL) [Low / Normal]

Respiratory Rate: 12 (breaths/minute)

Inspiratory Pressure Limit: 35 (cm H_2O)

Inspiratory:Expiratory Ratio:: 1:2

	1st ABG	2nd ABG
Time of collection		
Concomitant $ETCO_2$ (mm Hg)		
F_iO_2 (%)		
pH		
P_aO_2 (mm Hg)		
P_aCO_2 (mm Hg)		
HCO_3^-		
S.B.E		
S_aO_2 (%)		

$ETCO_2$ Limits: 24 – 40 mm Hg

Did $ETCO_2$ go beyond the defined limits: Yes / No

Did $ETCO_2$ exceed or fall below the limts: Exceeded 40 mm Hg / Fell below 24 mm Hg

Time:	Respiratory Rate changed to:
Time:	Tidal Volume changed to:

Any sudden hemodynamic problems intra-operatively (specify with details of occurrence, time, management, and outcome):

APPENDIX C: PATIENT INFORMATION SHEET

EVALUATION OF THE INCIDENCE OF INADEQUATE VENTILATION WITH TIDAL VOLUMES OF 6 ML/KG AND 10 ML/KG DURING GENERAL ANAESTHESIA IN OVERWEIGHT OR OBESE ADULTS.

You are about to undergo surgery, for which general anaesthesia will be optimum. General anaesthesia means you will be unconscious during the surgery. The job of the anaesthetist will be to keep you asleep, pain-free and healthy during the operation, and ensure a safe recovery from anaesthesia. This is done with the help of various medications and the anaesthesia machine which provides for your breathing needs.

Normally, an awake patient breathes in about10 mL of air per kilogram of body weight with each breath. Under anaesthesia, changes occurring to body position and breathing pattern result in collapse of peripheral airways in the lungs. This collapse of airways occurs even when the breathing is controlled by the anaesthesia machine. We are conducting a study to find out if more collapse of airways occurs when smaller volumes of gas are delivered by the machine with each breath.

This study will help us treat patients in the following ways:

1) There is a small risk of damage to the lungs even while using normal breathing volumes. This can be avoided if it is found that smaller breathing volumes do not cause more collapse of airways;
2) However, if smaller breathing volumes do cause more collapse of airways, this method should be avoided as the collapse of airways itself can cause problems of decreased oxygen in the blood

How are you involved in this study:

If you consent to participate in this study, you will be randomly allocated to receive either 6 mL/kg or 10 mL/kg of gas mixture with each mechanical breath during anaesthesia. You will not be informed of which group you will be placed in. For example, if your height is 160 cm.,

your ideal body weight would be 56 kg. If you are supposed to receive 6 mL/kg, you will receive around 336 mL of gas mixture with each breath; and if you are supposed to receive 10 mL/kg, you will receive around 560 mL of gas mixture with each breath.

Both 6 mL/kg and 10 mL/kg are being used currently in anaesthesia. It is our aim to find out which one is better for our patients.

Anaesthesia will be provided in a safe, routine, and internationally accepted manner. While you are unconscious, two blood samples will be collected from you to provide the information we are seeking. As you will be unconscious, you will not feel any pain from the injections. The first sample will be collected immediately after you are unconscious, and the second, two hours later. The sites from which blood samples are collected will be cleaned and compressed adequately.

The risks you face from enrolling in this study are negligible. After blood sample collection, there is an extremely small risk of blockage of the blood vessel or of bleeding, both of which are avoided by the use of a very small needle and proper compression, which we will ensure.

At the end of two hours, your involvement in the project will be complete. If we find from the blood samples that any abnormalities are present, they will be treated immediately and free of cost to you. There is no additional cost to you from this study. You will only be paying the routine costs for anaesthesia, which you would be paying even if you were not taking part in this study.

We are hoping to make the results of this study public but no personal identification details of any patient joining this study will be divulged.

Please note that all the steps involved in this project are routinely performed in the operation theatre, including the method of anaesthesia, mechanical breathing, and blood sample collection. These are not unknown, new, or controversial procedures.

APPENDIX D: CONSENT FORM

EVALUATION OF THE ADEQUACY OF VENTILATION WITH TIDAL VOLUMES OF 6 ML/KG AND 10 ML/KG DURING GENERAL ANAESTHESIA IN OVERWEIGHT OR OBESE ADULTS.

I, _____ (Hospital No.:_____), do hereby give my consent to be enrolled in the study termed "Evaluation of the incidence of inadequate ventilation with tidal volumes of 6 mL/kg and 10 mL/kg during general anaesthesia in overweight or obese adults."

I have been given a copy of the Patient Information Sheet in a language that I understand and it has been explained to me. I have been given adequate time to ask questions and they have been answered to my satisfaction. [ ]

I make this decision to be enrolled in this study freely, of my own volition, and without any external influence, coercion, or incentive. [ ]

I understand that refusal to enroll in this study will not affect the standard of care provided to me, and that I can withdraw myself from the study anytime. [ ]

By agreeing to be enrolled in this study, I give my consent for the following:

1) To be randomly (without my knowledge) allocated to receive either 6 mL/kg or 10 mL/kg (kg means kilograms of calculated ideal body weight) of gas mixture with each breath (tidal volume) for the first two hours of anaesthesia. [ ]
2) To have two blood samples collected (one at the beginning of anesthesia and another after two hours). [ ]

I understand that all usual standards of care will be followed during the study. [ ]

The potential risks to me have been explained. [ ]

I understand that any abnormalities detected during the study arising out of the study will be treated immediately and free of cost to me. However, the usual charges for anaesthesia will be added to my hospital bill. I will not receive any financial returns for taking part in this study, whether in terms of actual cash, or as a reduction in the hospital bill. [ ]

Signature _____ _____

(Study Participant) (Relation to Participant)

(Witness)

Investigator: _____

Date: _____

APPENDIX E: DATA SPREAD SHEET